AN NMR STUDY OF 2-ETHYL-1-BUTYLLITHIUM AND OF 2-ETHYL-1-BUTYLLITHIUM/LITHIUM 2-ETHYL-1-BUTOXIDE MIXED AGGREGATES

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A ^{1}H, ^{13}C, and ^{6}Li NMR study of 2-ethyl-1-butyllithium indicated that 2-ethyl-1-butyllithium exists only as a hexameric aggregate over the entire temperature range of 25 to – 92.1 °C in cyclopentane. Reacting 2-ethyl-1-butyllithium with 2-ethyl-1-butanol resulted in alkyllithium/lithium alkoxide mixed aggregates, apparently of the form $R_a(RO)_bLi_{a+b}$. A multinuclear, variable temperature NMR study of samples with O:Li ratios of 0.2 and 0.4 showed, in addition to the alkyllithium, the formation of four mixed aggregates, one of them probably an octamer. Higher O:Li ratio samples showed the formation of several other mixed aggregates. Mixing 2-ethyl-1-butyllithium with independently prepared lithium 2-ethyl-1-butoxide formed the same mixed aggregates formed by *in situ* synthesis of lithium alkoxide. Lithium 2-ethyl-1-butoxide also exists as aggregates in cyclopentane.

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CHAPTER I

INTRODUCTION

Alkyllithium compounds

Alkyllithium compounds form a special group of organometallic reagents that are used in various organic and organometallic syntheses.[1-3] One of their major applications in synthesis is the formation of new carbon-carbon bonds. They can also act as a strong base. Despite the fact that a variety of alkyllithium compounds are commercially available, their structure and behavior in solution are not always well known. Therefore, it is important to study these characteristics in order to establish their action in the syntheses for which they are used. Knowing their structures may also help to determine certain reaction mechanisms in which they are involved.

Studies have determined the structures of some of these compounds in the solid state through X-ray crystallography. Structures such as monomers, dimers, tetramers and hexamers have been observed in the solid state.[4-10] However, these compounds may have different structures in solution. Therefore, NMR spectroscopy is used to study these compounds in solution.[11-13] That is necessary since the reactions in which these compounds are involved occur in a liquid phase.

Alkyllithium compounds are usually represented by the simple formula RLi in reaction equations and in organic syntheses. However, these compounds are known to

exist as aggregates in solutions.[13-16] Therefore, a better representation would be as shown in equation 1, where n is the aggregation state.

$$n\ RLi \rightarrow (RLi)_n \quad (\text{with } n = 2, 3, 4, 6, 8, 9\ldots) \qquad [\text{eq. 1}]$$

The aggregation states of the alkyllithium compounds vary according to different factors such as the nature of the alkyl group, the temperature of the solution, the concentration of the solute and the nature of the solvent.[13] Also, more than one aggregate can exist in the same solution.[14]

When multiple aggregates are found in solution, varying the temperature can affect the equilibrium between different aggregate species. Normally, what is observed for non-coordinating solvents is that lowering the temperature favors the higher aggregation state. For instance, if a solution has a mixture of tetramers and hexamers at room temperature, at lower temperatures the larger aggregate may be favored and the proportion of hexamer to tetramer increases. The opposite effect has been observed in solutions with a coordinating solvent, that is, the higher the temperature, the larger the aggregate.

The concentration of the alkyllithium in solution can also affect the equilibrium between different aggregation states. As the concentration increases, the larger aggregate in the equilibrium is favored. The opposite is observed as the concentration decreases.

In non-coordinating hydrocarbon solvents, dimers, trimers, tetramers, hexamers, octamers and nonomers have been observed. Non-coordinating solvents favor higher

aggregation states. In contrast, coordinating solvents tend to lower the aggregation state. For example, tert-butyllithium, which is a tetramer in cyclopentane,[17] is known to be a monomer in THF and a dimer in diethyl ether.[18]

The nature of the alkyl group affects the aggregation state due to steric effects. If the alkyl groups are large bulky groups, the compound tends to have a low aggregation state. This is the case with tert-butyllithium, which is tetrameric in hydrocarbon solvent. On the other hand, smaller and less sterically hindered groups can form larger aggregates. For example, n-propyllithium exists as hexamers, octamers and nonomers in hydrocarbon solution.[14]

The ^{13}C NMR spectra of some alkyllithium compounds show coupling between the alpha carbon, which is directly attached to lithium, and the lithium nuclei. Aggregation states of fluxional alkyllithium compounds in solution have been assigned based on the multiplicity of the ^{13}C multiplet or on the magnitude of the observed coupling. The magnitude of the coupling was found from experimental data[18,19] to be approximately

$$J_{^{13}C,^{6}Li} = (17 \pm 2\ \text{Hz}) / n \qquad \text{[eq. 2]}$$

where n is the number of equivalent ^{6}Li nuclei to which the carbon is coupled. In a fluxional aggregate, n is also the aggregation state.

This formula can be used as a good approximation, but it is not precise enough to give a definite assignment. Other methods should be used to corroborate the assignment such as a line shape analysis of the multiplet of the alpha carbon. The line shape analysis can help determine the multiplicity of the ^{13}C multiplet by comparing the number of lines

that can be observed in the experimental multiplet and their intensities with a few different simulated multiplets where the aggregation state is varied. Sometimes, the most outside lines of a multiplet can not be observed because of the great difference in the intensities between all of the peaks in that multiplet. This is also a factor in the simulation, and according to how fast the outside lines are decreasing, some multiplets can be ruled out in comparison with the experimental data.

Alkyllithium/lithium alkoxide mixed aggregates

Alkyllithium compounds can react with oxygen or alcohol to form alkoxides, as represented in equations 3 and 4.

$$2\ RLi + O_2 \rightarrow 2\ ROLi \qquad \text{[eq. 3]}$$

$$RLi + ROH \rightarrow ROLi + RH \qquad \text{[eq. 4]}$$

Commercially available alkyllithium compounds are very likely to have some lithium alkoxides present due to oxygen contamination during their handling and used. The presence of these lithium alkoxides is important because they can affect the reactivity of the alkyllithium compounds, more likely increasing it. As the alkyllithium compounds form aggregates in hydrocarbon solutions, the lithium alkoxides are likely to form aggregates too. When both compounds are present in the same solution, they may form alkyllithium/lithium alkoxide mixed aggregates, depending on the characteristics of

the mixed solution. Therefore, the study of these mixed aggregates is important to better understand the reactivity of these compounds.

Samples containing both alkyllithiums and lithium alkoxides, obtained via *in situ* synthesis of an alkyllithium reacting with alcohol, have been studied and alkyllithium/lithium alkoxide mixed aggregates have been identified.[20-24] Reacting an alkyllithium compound with alcohol as shown in equation 4, the formation of lithium alkoxides can be controlled. Depending upon the amounts of the alkyllithium and alcohol being used, the final products in solution will have different concentrations. If the amount of alcohol used is less than the equivalent molar amount of alkyllithium, the final result will be a mixture of alkoxide, alkane and the alkyllithium left unreacted. Increasing the amount of alcohol, more and more alkoxide will be formed and less and less alkyllithium will be left until all the alkyllithium is converted to alkoxide. Therefore, with alkyllithium and lithium alkoxide compounds in solution, mixed aggregates are expected to form and to have the general formula shown in equation 5.

$$a\ RLi + b\ ROLi \rightarrow R_a(RO)_bLi_{a+b} \qquad \text{[eq. 5]}$$

The presence of the alkoxide groups in these mixed aggregates is observed to increase the size of the aggregate. t-Butyllithium, which is tetrameric in cyclopentane, reacts with the corresponding alcohol to form both tetrameric and hexameric t-butyllithium/lithium t-butoxide mixed aggregates.[23] The mixed hexamers have the form $R_n(RO)_{6-n}Li_6$, with n = 1,2 and R = t-butyl, while the mixed tetramer is $(RO)R_3Li_4$. The

addition of an oxygen atom increases the spacing between the lithium and the steric bulky alkyl group, making possible the formation of larger aggregates.

The n-butyllithium is one of the alkyllithium compounds used for many applications, making it important to study its mixed aggregates. However, NMR studies of straight-chain alkyllithium compounds in solution were not able to show ^{13}C-^{6}Li coupling for n-butyllithium compounds and for larger carbon chains.[16] One compound for which coupling can be observed is the n-propyllithium, which has been used as a model for the other straight-chain compounds. Mixed solutions of n-propyllithium and n-propyl alcohol have been studied, and a new dodecameric n-propyllithium/lithium n-propoxide mixed aggregate has been reported.[24] This is the largest alkyllithium/lithium alkoxide mixed aggregate observed thus far.

Lithium hydride/lithium alkoxide mixed aggregates

A different group of mixed aggregates has been studied recently. The alkyl groups within the alkyllithium/lithium alkoxide mixed aggregates more readily undergo beta-hydride elimination to form a new type of mixed aggregate, lithium hydride/lithium alkoxide mixed aggregates. This process formed larger aggregates than just the original alkyllithium or the alkyllithium/lithium alkoxide, as it has been reported for the lithium hydride/lithium t-butoxide aggregate.[25] Two mixed aggregates of lithium hydride/lithium t-butoxide were observed and assigned as a decamer and a dodecamer, respectively, with only one hydride per aggregate. Therefore, these aggregates are represented by the general formula $(RO)_{m-1}HLi_m$, with m = 10 and 12 for R = t-butyl. Two different

processes produced these mixed aggregates, the thermal and the photochemical decomposition of the alkyllithium/lithium alkoxide mixed aggregate.

2-ethyl-1-butyllithium and its mixed aggregates

The objective of this research is the study of a primary system, which has a primary carbon from the alkyl group attached to the lithium, but with a beta branching on the alkyl group. The preliminary studies of primary, straight-chain alkyllithium systems have found multiple aggregates in solution.[16,17] The branching is intended to avoid the formation of higher aggregation states by adding a steric effect to the alkyl group. Consequently, fewer aggregates are expected to form. Ideally, only one aggregate would be formed, making it be easier to study its properties.

The compound chosen for this research was the 2-ethyl-1-butyllithium, which has a primary carbon attached to the lithium and an ethyl branching on the beta-carbon. This compound has a plane of symmetry that makes the two ethyl ends chemically and, more importantly, magnetically equivalent. This is very important feature in this compound that makes the ^{1}H and ^{13}C NMR spectra cleaner because fewer signals will be observed, therefore, less chance for overlap of peaks. The study of the mixed aggregates containing alkyl and alkoxides groups is possible by adding certain amounts of the corresponding alcohol to the alkyllithium solution. This procedure promotes the exchange of some alkyl groups by the alkoxides, forming the mixed aggregates.

This thesis presents the study of the 2-ethyl-1-butyllithium in cyclopentane solution and the formation of mixed aggregates upon reacting with its corresponding

alcohol, 2-ethyl-1-butanol. This specific alcohol was chosen so that both alkyl and alkoxide have the same R group. Having the same R group is one way to prevent contaminant's interference. If the sample were exposed to oxygen, the alkyllithium would be converted to lithium alkoxide alkoxide by the addition of an oxygen atom. When the alcohol has the same R group, it produces the same alkoxide as the oxygen contamination. This ensures that sample has only one type of alkoxide, which helps in the investigation of the mixed aggregates. The lithium 2-ethyl-1-butoxide was also prepared independently so that some qualitative data could be obtained and compared with the data from the mixed solution.

CHAPTER BIBLIOGRAPHY

1. Wakefield, B. J., *The Chemistry of Organolithium Compounds*, Pergamon Press, Oxford, 1974.

2. Wakefield, B. J., *Organolithium Methods*, Academic, Oxford, 1988.

3. Wardell, J. L., *Comprehensive Organometallic Chemistry*, Wilkinson, G. Ed.; Pergamon Press: New York, 1982, Vol 1, 43.

4. Weiss, E. *Angew Chem., Int. Ed. Engl.* **1993**, *32*, 1501.

5. Gorrell, I. B. *Annu. Rep. Prog. Chem., Sect. A: Inorg. Chem.* **1994**, *90*, 3.

6. Olsher, U.; Izatt, R. M.; Bradshaw, J. S.; Dalley, N. K. *Chem. Rev.* **1991**, *91*, 137.

7. Schleyer, P. v. R.; Gregory, K.;Snaith, R. *Adv. Inorg. Chem.* **1991**, *37*, 47.

8. Seebach, D. *Angew. Chem, Int. Ed. Engl.* **1988**, *27*, 1624.

9. Schiemenz, B.; Power, P. P. *Agnew. Chem. Int. Ed. Engl.*, **1996**, *35*, 2150.

10. Kottke, T.; Stalke, D. *Agnew. Chem. Int. Ed. Engl.*, **1993**, *32*, 580.

11. Fraenkel, G.; Hsu, H.; Su, B. M. In *Lithium: Current Applications in Science, Medicine and Technology*; Bach, R. O., Ed.; John Wiley & Sons: New York, 1985, 273.

12. Bauer, W. In *Lithium Chemistry: A Theoretical and Experimental Overview*; Sapse, A. M.; Schleyer, P. v. R., Eds.; John Wiley & Sons: New York, 1995, 125.

13. Thomas, R. D. In *Isotopes in the Physical and Biomedical Sciences;* Buncel, E.; Jones, J. R., Eds.; Elsevier, Amsterdam, 1991, 2, 367.

14. Fraenkel, G.; Henrichs, M.; Hewitt, J. M.; Su, B. M.; Geckle, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 3345.

15. Fraenkel, G.; Henrichs, M.; Hewitt, J. M.; Su, B. M.; *J. Am. Chem. Soc.* **1984**, *106*, 255.

16. Thomas, R. D.; Jensen, R. M.; Young, T. C., *Organometallics* **1987**, *6*, 565.

17. Thomas, R. D.; Clarke, M. T.; Jensen, R. M.; Young, T. C. *Organometallics* **1986**, *5*, 1851.

18. Bauer, W.; Winchester, W.; Schleyer, P. v. R. *Organometallics* **1987**, *6*, 2371.

19. Bauer, W.; Feigel, M.; Muller, G.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1988**, *110*, 6033.

20. Nguyen, H. D. Ph. D. Dissertation, University of North Texas, Denton, TX, 1997.

21. DeLong, G. T. Ph. D. Dissertation, University of North Texas, Denton, TX, 1992.

22. Thornton, T. L. Master Thesis, University of North Texas, Denton, TX, 1997.

23. DeLong, G. T; Pannell, D. K.; Clarke, M. T.; Thomas, R. D. *J. Am. Chem. Soc.* **1993**, *115*, 7013.

24. Thomas, R. D.; Huang, H. *J. Am. Chem. Soc.* **1999**, *121*, 11239.

25. DeLong, G. T.; Hoffmann, D.; Nguyen, H. D.; Thomas, R. D. *J. Am. Chem. Soc.* **1997**, *119*, 11998.

CHAPTER II

EXPERIMENTAL

Introduction

The alkyllithium used in this study had been synthesized previously by other members in the research group. Connie Wang started the synthesis and Daniel Lin carried out the last step. The reactions 1 through 3 represent the synthetic steps used to obtain the final product.

$$RX + Mg \rightarrow RMgX \qquad \text{[eq. 1]}$$

$$2\ RMgX + HgX_2 \rightarrow HgR_2 + 2\ MgX_2 \qquad \text{[eq. 2]}$$

$$HgR_2 + 2\ Li \rightarrow 2\ RLi + Hg \qquad \text{[eq. 3]}$$

The synthesis was carried out through the alkylmercuration to avoid contamination of other lithium by-products such as lithium halides. The presence of lithium halides could interfere with the structural analysis of the alkyllithium compound because it could become part of the aggregates. A 95.5 % isotopically enriched ^{6}Li metal (U.S. Services) was used in equation 3. Experimental details of these synthetic steps have been described elsewhere.[1,2]

The original 2-ethyl-1-butyllithium obtained had been stored in a sealed vessel and kept refrigerated. To determine that this sample in particular was still good, a 2 M solution in cyclopentane was prepared and analyzed.

The ^{13}C NMR spectrum showed peaks at 10.87, 19.39, 25.89, 31.59 and 42.21 ppm that are consistent with reported values for this compound,[3] while the peak at 25.89 ppm is due to the cyclopentane solvent. The ^{6}Li NMR spectrum showed only one peak, which suggests that there were no lithium alkoxides or other lithium compounds. Therefore, the 2-ethyl-1-butyllithium was considered acceptable for this study. Further discussion about these spectra is present in the next Chapter.

Because this compound is very sensitive to oxygen and moisture, it was always handled in the inert atmosphere of an argon-filled dry box (glove-box) or under high vacuum, $\leq 5x10^{-6}$ torr. Once in the presence of oxygen, the compound would react to form the corresponding alkoxide (equation 4).

$$2\ RLi\ +\ O_2\ \rightarrow\ 2\ ROLi \qquad \text{[eq. 4]}$$

In order to preserve the original compound from being contaminated or degraded through reactions as described above, the compound was manipulated with extreme care and caution, so as not to compromise the integrity of the material. The procedures used to assure the proper manipulation are described below.

Precautions and procedures to handle the alkyllithium

The original alkyllithium compound was always handled in an argon-filled dry box. This is a crucial precaution to prevent the compound from being exposed to air and moisture. Such exposure would cause the compound to decompose to alkoxides and hydroxides. The presence of alkoxides due to contamination or exposure would prevent the collection of good data about the alkyllithium in study.

All glassware to be used on the vacuum line was checked under a vacuum of $\leq 5x10^{-6}$ torr to ensure that there were no holes. The glassware was then dried in a conventional oven for at least two hours and placed in the dry box's anti-chamber while still hot. An alternative method sometimes used was to place the hot glassware into a desiccator to cool, and then transfer the glassware to the anti-chamber. These procedures were used to prevent the glassware from absorbing moisture before being placed inside the dry box.

After closing the anti-chamber's outside door, the anti-chamber was evacuated. The next step was filling the anti-chamber with argon from the dry box and then evacuating again. This cycle of evacuating and re-filling the anti-chamber was repeated at least three times. Finally, the anti-chamber was filled with argon one last time to equalize the pressure, so that the inside door could be opened and the material could be brought inside the box. The dry box was equipped with a system containing a catalyst capable of removing oxygen and water. This system consisted of alternating layers of Alpha De-Ox oxygen removal catalyst (Alpha Products) and type 5A molecular sieves (Fisher Scientific). The argon was constantly circulated through this system. The catalyst was

regenerated from time to time to avoid its saturation and to ensure that it was functioning properly and keeping the atmosphere inside the box inert. The regeneration was always done before the manipulation of the compounds when preparing the samples. After the regeneration of the catalyst, the conditions of the box were assumed to have improved and the dry box was good to be used. A light bulb burning inside the box is a recommended test that could be used to ensure the cleanliness of the atmosphere inside the box.

Preparation of the standard NMR solvent and other reagents

The solvent used in the NMR samples was a mixture of protonated and deuterated cyclopentane. The presence of deuterated solvent is necessary for the NMR experiments. The deuterium provides the lock signal during the spectrum acquisition. However, the use of only deuterated cyclopentane is prohibitively expensive, and the mixture was used instead.

The deuterated cyclopentane (99.5% atom D, CDN Isotopes) was weighed on an analytical balance and 4.5615g were added to a 250 mL Erlenmeyer fitted with a ground male joint. The protonated cyclopentane (99.5% pure, Fluka Chemika) was weighed and 40.7752g were added to the same flask. The amounts used results in a mixture that is 10.06% C_5D_{10} in C_5H_{10}, which was adequate for the NMR experiments. The drying agent used was $LiAlH_4$, and about 0.9g was also added to the flask, which was capped with a stopcock. After keeping the mixture drying overnight, the flask was put on the vacuum line.

The solvent mixture was frozen with liquid nitrogen and then the flask was evacuated. After evacuation of the flask, the stopcock was closed and the solvent was allowed to melt. This process causes the solvent to be degassed, and the cycle of freezing-pumping-thawing was repeated as needed until no more gas came out of the liquid. The mixture was degassed four times. The next step was to transfer the solvent to a storage vessel, which was brought inside the dry box. The storage vessel had a rotaflo valve and a neck with 14/35 male ground joint that connected to the vacuum line. The solvent was transferred over a closed and evacuated portion of the vacuum line with the vessel being kept at liquid nitrogen temperature and the solvent thawing in the original flask. With this procedure, only the solvent was transferred from the original flask to the storage vessel, and, therefore, the solvent was separated from the drying agent. The storage vessel was closed and ready to be taken inside the dry box.

The 2-ethyl-1-butyl alcohol, used to prepare some samples and also used for the synthesis of the alkoxide, was also handled very carefully. The alcohol was distilled at 146°C into an Erlenmeyer equipped with a male ground joint, where it was allowed to dry over calcium hydride for more than one day. Later, the Erlenmeyer flask was put on the vacuum line so that the alcohol could be transferred to a clean storage vessel. The alcohol also was degassed and the storage vessel was taken inside the dry box and kept there for future use.

Preparation of the NMR samples[4]

The samples used in this study were samples of the alkyllithium, 2-ethyl-1-butyllithium, and mixtures of the alkyllithium with the corresponding alcohol, 2-ethyl-1-butanol. Mixing the alkyllithium and alcohol would lead to the formation of the lithium alkoxide, lithium 2-ethyl-1-butoxide, according to equation 5.

$$RLi + ROH \rightarrow ROLi + RH \qquad \text{[eq. 5]}$$

All samples were prepared to be 2 F in concentration in cyclopentane (i.e. 2 M based on monomeric alkyllithium). The mixed aggregate samples were prepared using approximately the same amount of the pure alkyllithium sample, but different amounts of alcohol were added to achieve different ratios of oxygen to lithium. The samples were prepared using a simple procedure of weighing the compound and adding solvent. However, extreme care was taken to avoid contamination.

The alkyllithium sample was prepared as follows. Inside the dry box, 0.130 g (1.43×10^{-3}mol) of 2-ethyl-1-butyllithium was weighed into a 10 mL beaker and about 0.5 mL of the NMR solvent was added to dissolve the compound. The solution was then transferred via pipette to a 5 mm NMR tube equipped with a 14/35 male joint. Some more solvent was added to wash the beaker and the pipette and then added to the NMR tube to complete the amount of solvent needed. The NMR tube was marked so the volume of sample corresponded to 0.7 mL and this volume was used to calculate the concentration of the samples. The NMR tube was then capped with a stopcock and taken

outside of the dry box. This sample tube was then put in the vacuum line and the solution was degassed at least three times before the tube was flamed sealed.

The mixed aggregate samples were prepared with the following procedure. Inside the dry box, the alkyllithium, 2-ethyl-1-butyllithium, was weighed into a 10 mL beaker and about 0.35 mL of the NMR solvent was added. In another 10 mL beaker, the alcohol, 2-ethyl-1-butanol, was weighed and also diluted with about 0.35 mL of the NMR solvent. The amounts used are listed in Table 1.

Table 1 – Amounts of alkyllithium and alcohol used in the samples (all samples intended to be 2 F in cyclopentane).

O/Li ratio	**Amount of Alkyllithium** (2-ethyl-1-butyllithium)	**Amount of Alcohol** (2-ethyl-1-butanol)
0/1 (just alkyllithium)	0.130 g (1.43×10^{-3}mol)	Not used
0.2/1	0.135 g (1.48×10^{-3}mol)	0.028 g (2.74×10^{-4}mol)
0.4/1	0.129 g (1.42×10^{-3}mol)	0.060 g (5.87×10^{-4}mol)
0.6/1	0.138 g (1.51×10^{-3}mol)	0.085 g (8.32×10^{-4}mol)
1/1	0.128 g (1.40×10^{-3}mol)	0.142 g (1.39×10^{-3}mol)

The alcohol solution was then transferred drop by drop to the beaker containing the alkyllithium solution, preferably running the drop down the beaker wall instead of letting it fall directly into the solution. This transfer was made very slowly and carefully, because the alcohol reacted exothermally with the alkyllithium. After each drop of the

alcohol solution was added, the beaker was swirled for a couple times before the next drop was added. This procedure was followed to avoid high local concentration of the alcohol and also to avoid too much heat from being generated from the reaction between the alcohol and alkyllithium. This was very important because excessive heat could cause some decomposition of the final products.

After the alcohol solution had been transferred, the mixture of the alkyllithium and alcohol was transferred to a 5 mm NMR tube equipped with a male ground joint. Some of the solvent evaporated because of the heat, therefore, more solvent was added to the beaker and transferred to the tube until the 0.7 mL mark was reached. In the same fashion, the NMR tube was capped with a stopcock, taken outside of the dry box, put on the vacuum line and the solution was degassed at least three times before the tube was flamed sealed.

Independent synthesis of lithium 2-ethyl-1-butoxide

The lithium 2-ethyl-1-butoxide was prepared independently of the original 2-ethyl-1-butyllithium according to the following reaction (equation 6). Similar syntheses have been described elsewhere.[4]

$$^{6}Li + HOCH_2CH(CH_2CH_3)_2 \rightarrow {}^{6}LiOCH_2CH(CH_2CH_3)_2 + \tfrac{1}{2} H_2 \qquad \text{[eq. 6]}$$

All glassware used was dried in a conventional oven at 200°C, and then allowed to cool under argon flow. The solvent used for the reaction was cyclopentane, which had

been dried over calcium hydride (CaH_2). Approximately 50 mL of cyclopentane was distilled into a three-neck 500 mL round bottom flask that was kept under argon flow. A magnetic stirring bar was added and the flask was closed with rubber septa, fastened with wire. The flask was taken into the dry box where approximately 0.25 g (0.0416 mol) of enriched ^{6}Li was cut and added to the flask. The flask was then taken out of the dry box and attached to an argon source through one of the necks. The middle neck was equipped with a condenser that was capped with a bubbler to allow the argon to flow and also to release any pressure build up during the reaction. The other neck was still closed with a rubber septum.

The system was flushed with argon for about 20 minutes and then the flow was stopped. Next, the system was heated and allowed to reflux with constant stirring, and 1.5 g (0.0146 mol) of dried 2-ethyl-1-butanol was injected to the reaction flask with a syringe through the rubber septum. The solution was allowed to reflux for approximately 9 hours. A white precipitate formed, but it remained suspended in the solvent. After the reaction mixture was allowed to cool to room temperature, the solution with the precipitate was transferred to an Erlenmeyer via a cannula, using positive argon pressure, so the mixture was separated from the unreacted pieces of lithium. The Erlenmeyer flask to which the solution was transferred had been flushed with argon before. This flask, equipped with a male ground joint, was closed with a stopcock and put on the vacuum line where the solvent was removed, leaving a yellowish-white solid.

The flask containing only the solid, presumably lithium 2-ethyl-1-butoxide, was taken inside the dry box and then opened. The solid was removed from the walls of the

flask and 0.153 g (0.00143 mol) was weighed and added to a 10 mL beaker. Approximately 0.7 mL of the NMR solvent, the mixture of C_5D_{10} in C_5H_{10} (10% by weight), was added to dissolve the solid, producing a concentration of approximately 2 F. Even though the solution seemed to have a large amount of insoluble precipitate, it was transferred to an NMR tube equipped with a 14/35 male ground joint that was then capped with a stopcock. The tube was taken out of the dry box and put on the vacuum line, and, after three pump-freeze-thaw cycles, it was flamed sealed. With time, more of the solid seemed to dissolve in the solution, but a large amount of solid was still present. After sitting for one day, the solid had agglutinated and it was floating on top of the solvent, leaving a clear yellowish solution at the bottom of the sealed tube. This NMR tube was used to obtain the chemical shifts of the lithium 2-ethyl-1-butoxide.

Another sample was prepared by mixing 2-ethyl-1-butoxide with 2-ethyl-1-butyllithium. The preparation of this sample involved the weighing of the compounds in 10 mL beakers followed by the addition of the standard NMR solvent. The amounts used are listed in Table 2.

Table 2 – Amounts of lithium alkoxide and alkyllithium used in the samples (all samples intended to be 2 F in cyclopentane).

O/Li ratio	**Amount of Lithium Alkoxide** (2-ethyl-1-butoxide)	**Amount of Alkyllithium** (2-ethyl-1-butyllithium)
1/1 (just lithium alkoxide)	0.153 g (1.43×10^{-3} mol)	Not used
0.2/1	0.030 g (2.80×10^{-4} mol)	0.103 g (1.13×10^{-3} mol)

The solutions were mixed together and transferred to a 5 mm NMR tube. This sample also presented some insoluble precipitate as did the pure lithium alkoxide sample, but less precipitate was observed due to the smaller amount of 2-ethyl-1-butoxide used.

Description of the NMR experiments

All NMR experiments were obtained using a Varian® VXR-300 spectrometer, with resonance frequencies of approximately 300 MHz, 75 MHz and 44 MHz, for proton (^{1}H), carbon (^{13}C) and lithium (^{6}Li), respectively.

All the NMR tubes prepared were 5 mm in diameter even though the probes used in the spectrometer had two different sizes, 5 mm and 10 mm. The 5 mm probe used was a regularly manufactured multi-element tunable probe, with three different coils: the decoupler coil, the observe coil and the lock coil.

The other probe used was a 10 mm custom made probe where the lock coil was substituted by a ^{6}Li decoupler coil that was used in conjunction with a frequency synthesizer. This enabled the spectrometer to perform some special experiments such as acquiring a ^{13}C spectrum with simultaneously decoupling of ^{1}H and ^{6}Li. Another experiment is the ^{13}C spin-echo with ^{6}Li decoupling,[5] which is used to differentiate between different types of aggregates. Details of this probe and other new experiment techniques that can be applied is described elsewhere.[6]

Most of the spectra were acquired using the 5 mm probe and the usual acquisition parameters are listed below. For a ^{1}H NMR spectrum, the spectral width was about 2000 Hz, the acquisition time was 2 seconds, the pulse width was 2 μs, and it was run with 16

transients. For a ^{13}C NMR spectrum, the spectral width was about 6500 Hz, the acquisition time was from 0.8 to 1 seconds, the pulse width was 4.9 μs, and it was run for about 3000 transients on average. For a ^{6}Li NMR spectrum, the spectral width was about 500 Hz, the acquisition time was 9.9 seconds with a delay of 30 seconds between scans, the pulse width was 10 μs, and it was run for 16 transients.

For both ^{6}Li and ^{13}C NMR spectra, the acquisition was normally run with broad band ^{1}H decoupling, but some ^{6}Li NMR spectra were run with gated decoupling so that lithium nuclei coupled to hydride ions were identified. The gated decoupled sequence of this experiment had the ^{1}H decoupler turned on during a delay in between scans, which helps to increase the signals due to NOE, but it was turned off during the acquisition time so that a coupled spectrum was obtained. The ^{6}Li NMR spectra used to determine the integration of the peaks were run with the ^{1}H decoupler turned off during all times to prevent NOE from building up, which would affect differently the intensity of the peaks.

The ^{1}H and ^{13}C NMR spectra have been referenced to TMS by assigning the solvent, cyclopentane, peaks to 1.51 ppm and 25.89 ppm, respectively. The ^{6}Li NMR spectra were referenced using a standard sample of tert-butyllithium in cyclopentane and assigning its peak to 0 ppm.

The 2D heteronuclear NOE correlated NMR spectroscopy (HOESY) was used to determine correlation between proton and lithium nuclei. In this study, the 2D $^{6}Li,^{1}H$-HOESY NMR experiment was performed with spectral windows of approximately 120 Hz and 1600 Hz for the ^{6}Li (in F2 dimension) and ^{1}H (in F1 dimension), respectively. The ^{6}Li 90° and 180° pulse used were 20.8 and 41.6 μseconds. The acquisition time was

1.33 seconds, the number of transients was 16, the delay time D1 was 3 seconds, and the mixing time was 2 seconds. The ^{1}H polarization transfer pulse (PP) was 19.4 μseconds, and the number of increments was 128.

The ^{6}Li J-modulated ^{13}C spin-echo pulse sequence[5] was performed with a spectral window of 6435 Hz. The ^{13}C 90° and 180° pulses used were 20.8 and 41.6 μseconds. The delay time D2 must equal $1/J_{obs}$ (J_{obs} = experimental ^{6}Li-^{13}C coupling observed) to refocus the peak. Therefore, D2 was set up as an array with 0, 0.314, 0.418, 0.470 and 0.625 seconds, so that the first spectrum had all ^{13}C peaks and the following spectra would refocus the carbon peaks that were coupled to six, eight, nine and twelve lithium nuclei, respectively.

For the low temperature spectra, the temperature of the probe was calibrated using a methanol sample,[7] because there were deviations from the temperature readings from the instrument and the real temperature felt by the sample inside the probe. The VXR-300 has a program that calculates the real temperature of the sample inside the probe based on the distance separation of the peaks present in a ^{1}H NMR spectrum of a methanol sample, which is temperature dependent. Therefore, to be sure of the temperature that the experiment was run, a temperature calibration was performed before each low temperature experiment. With the methanol sample inside, the temperature would be set to a chosen value and the probe allowed to reach the temperature. After about 15 min that the temperature had become stable, a ^{1}H NMR spectrum was acquired and the real temperature calculated. Then, the NMR sample was switched with the methanol sample

and allowed to stabilize for at least 15 minutes to assure that the sample temperature had been brought down to the temperature that was calculated.

CHAPTER BIBLIOGRAPHY

1. Thomas, R. D.; Jensen, R. M.; Young, T. C., *Organometallics*, **1987**, *6*, 565.

2. Thomas, R. D.; Clarke, M. T.; Jensen, R. M.; Young, T. C., *Organometallics*, **1986**, *5*, 1851.

3. Thomas, R. D.; Clarke, M. T.; Young, T. C., *J. Organometal. Chem.*, **1987**, *328*, 239.

4. Nguyen, H. D. Ph. D. Dissertation, University of North Texas, Denton, TX, 1997.

5. Thomas, R. D.; Ellington, D. H., *Magnetic Resonance in Chemistry*, **1989**, *27*, 628.

6. Ellington, D. H. Ph. D. Dissertation, University of North Texas, Denton, TX, 1990.

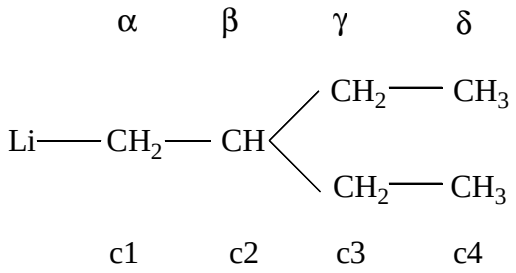
7. Van Geet, A. L. *Anal. Chem.* **1968**, *40*, 2227.

CHAPTER III

RESULTS AND DISCUSSION

2-Ethyl-1-butyllithium

2-Ethyl-1-butyllithium was the first sample analyzed. A basic representation of this compound is presented below.



The carbon atoms in the alkyl group are labeled using the Greek alphabet as alpha, beta, gamma and delta and also numerically as carbons 1, 2, 3 and 4 (c1, c2, c3, c4). These labels will be used to identify the chemical shift assignments in the NMR spectra of this compound.

The 5 mm tube prepared as described in Chapter II was used to acquire ^{1}H, ^{13}C and ^{6}Li NMR spectra at room temperature and several other lower temperatures ranging down to – 92.1 °C.

The ^{1}H NMR spectrum at room temperature, shown in Figure 1, presents five different peaks. The singlet peak at 1.51 ppm corresponds to the protons in the cyclopentane solvent, and it is a very strong peak due to the large amount of protonated

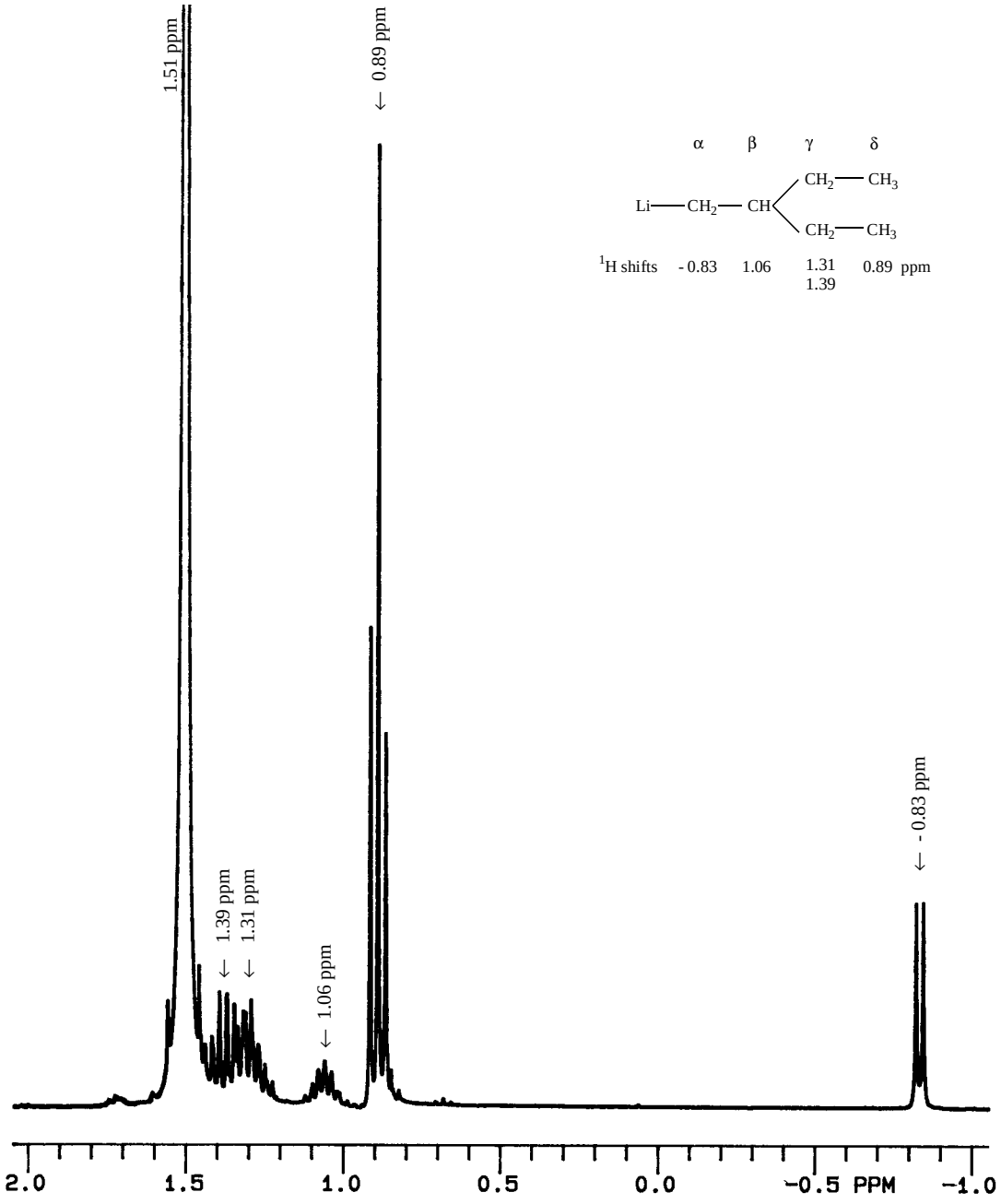


Figure 1 – ^{1}H NMR spectrum of 2-ethyl-1-butyllithium at room temperature. Inset shows the chemical shift assignments of this spectrum.

cyclopentane present in the sample. As was mentioned in Chapter II, the solvent used was a 9:1 mixture of protonated to deuterated cyclopentane.

The other peaks at 1.34, 1.06, 0.89 and – 0.83 ppm are the peaks for the protons on carbons c3, c2, c4 and c1, respectively. The multiplicity of the peaks helps to determine their assignments. The peak at 0.89 ppm is a triplet and the peak at – 0.83 ppm is a doublet, and, according to the splitting pattern of the proton signal, they should be coupled to two and one other proton nuclei, respectively. So, the 0.89 ppm triplet corresponds to the protons on c4 that are coupled only to the two protons on c3, and the coupling constant is 7.3 Hz. The upfield doublet at – 0.83 ppm corresponds to the protons on c1, the alpha carbon, which are coupled to the single proton on c2 with 6.8 Hz.

The other two peaks are complex multiplets. The 1.06 ppm peak appears to be a septet with broader lines. This peak is assigned to the proton on carbon c2 that is coupled to the two protons on c1 (J = 6.8 Hz) and the four protons from the two c3s. Considering that all protons on both c3s are magnetically equivalent and that their coupling constant are close to the coupling mention above, the proton in c2 is coupled to a total of six proton so that its signal should really be a septet. The coupling constants being close, but not quite the same, can explain the relative broadness of the lines in this multiplet.

The 1.34 ppm peak is a complex multiplet that must correspond to the protons on carbons c3, which is coupled to the protons on both carbons c2 and c4 (J = 7.3 Hz). However, this multiplet is difficult to be analyzed, and, in fact, there seems to be not just one multiplet, but two multiplets instead. This hypothesis can be explained considering that the two protons on both c3s have different chemical shifts due to them being in

different chemical environments. Because of the symmetry of the carbon chains in this compound, there would be two sets of two equivalent protons on the different c3s. Therefore, there would be two chemical shifts and also the coupling constants of these two set of protons with the proton on c2 would be different. Using a commercial computer software called gNMR[1] to perform a NMR spectrum simulation, one set of numbers that seems to fit the experimental spectrum is one set of proton at 1.39 ppm with 6.4 Hz coupling to the proton on c2, and the other set of protons at 1.31 ppm with 5.8 Hz coupling to the proton on c2. The simulation did not take into account the geminal coupling, which is a possibility since the protons have different chemical shifts, and, therefore, the numbers presented may not be accurate. This was considered a good approximation because the line shape of the simulation and the experimental spectrum were very similar, with the peaks in the multiplets showing the same chemical shifts and splitting. Data from a ^{1}H-^{13}C HETCOR spectrum supports this analysis because the c3 shows correlation to a relative large area in the ^{1}H NMR spectrum where the two peaks are assumed to be in the simulation presented.

This ^{1}H NMR spectrum indicates that only one type of alkyl group is present because no other peaks were observed. Consequently, there should be only one type of aggregate in this solution at this temperature, with the alkyl groups being magnetically equivalent to each other.

The ^{13}C NMR spectrum of this sample at room temperature, shown in Figure 2, reinforces the evidence for only one aggregate. This NMR spectrum shows only 5 peaks. For the same reason mentioned above, there is a strong solvent peak present in this

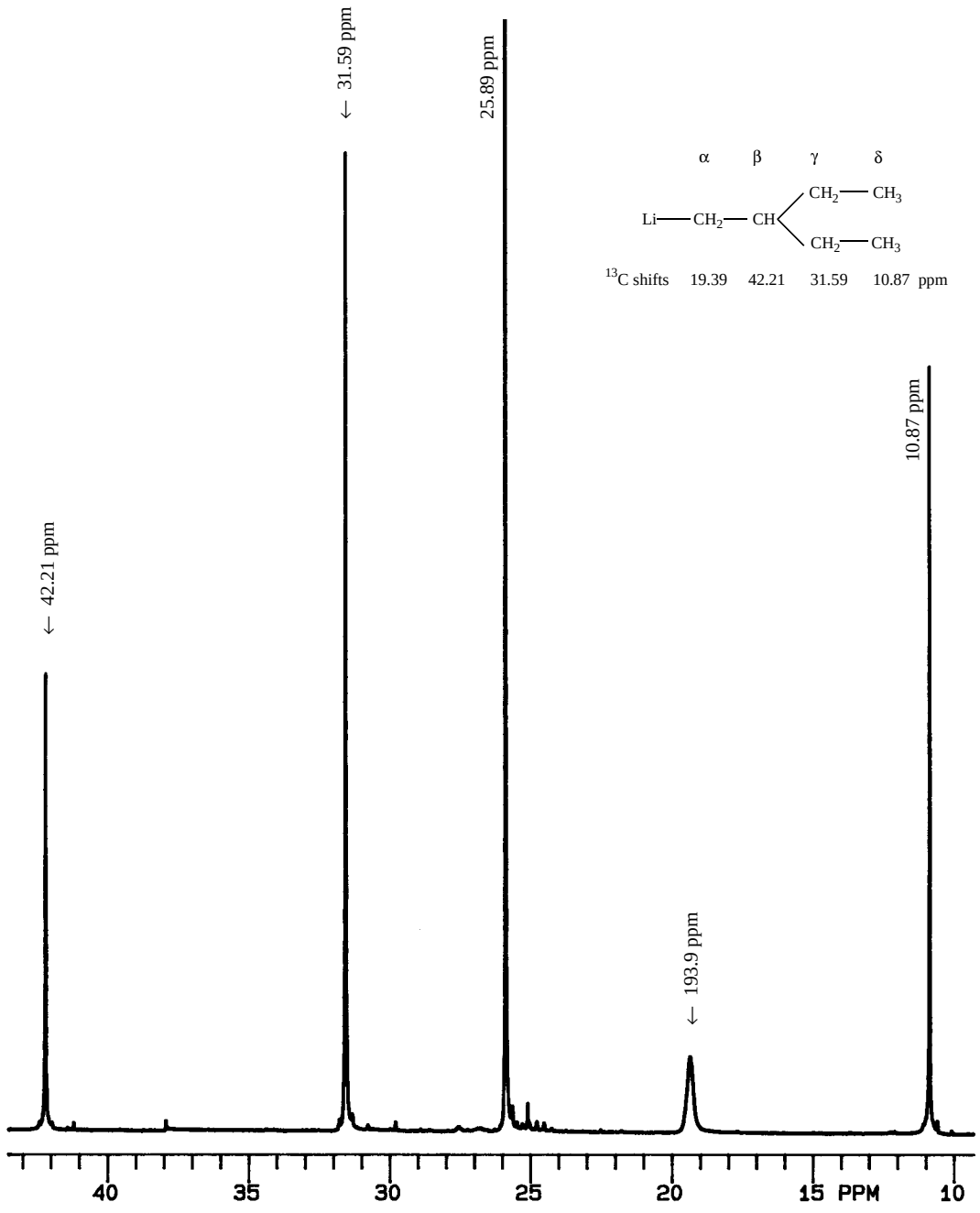


Figure 2 – ^{13}C NMR spectrum of 2-ethyl-1-butyllithium at room temperature. Inset shows the chemical shift assignments of this spectrum.

spectrum that is actually used as the reference peak, being assigned to 25.89 ppm relative to TMS. The other peaks present are at 42.21, 31.59, 19.39 and 10.87 ppm corresponding to the carbons c2, c3, c1 and c4, respectively, as it has been assigned previously.[2] All peaks are narrow single peaks due to ^{1}H broad band decoupling except for the alpha carbon peak at 19.39 ppm that appears as a small broad singlet at this temperature. The alpha carbon peak is broad due to unresolved coupling between the carbon and the lithium nuclei in the aggregate. At this temperature, the compound is probably undergoing fast interaggregate exchange of the alkyl groups. This makes the alpha carbon peak broad and no multiplet resolution can be obtained. These data are consistent with the hypothesis that there is only one aggregate at room temperature as mention above.

The ^{6}Li NMR spectrum at room temperature is shown in Figure 3. There is only one peak at 0.89 ppm downfield to the t-butyllithium sample that was used as an external reference at 0 ppm. This is further evidence that points to the existence of only one aggregate at room temperature. Also, the presence of just one peak indicates that all lithium nuclei are magnetically equivalent in the aggregate, and that there were no other compounds present in this solution.

2-Ethyl-1-butyllithium has been shown to exist as one aggregate undergoing rapid interaggregate and intraaggregate exchanges at room temperature. In an attempt to slow down these exchange processes, as had been done for other alkyllithium compounds,[3-5] NMR spectra were taken at several different low temperatures. The temperature ranged from room temperature down to – 92.1 °C for the ^{13}C NMR spectra and to – 87.4 °C for the ^{6}Li NMR spectra.

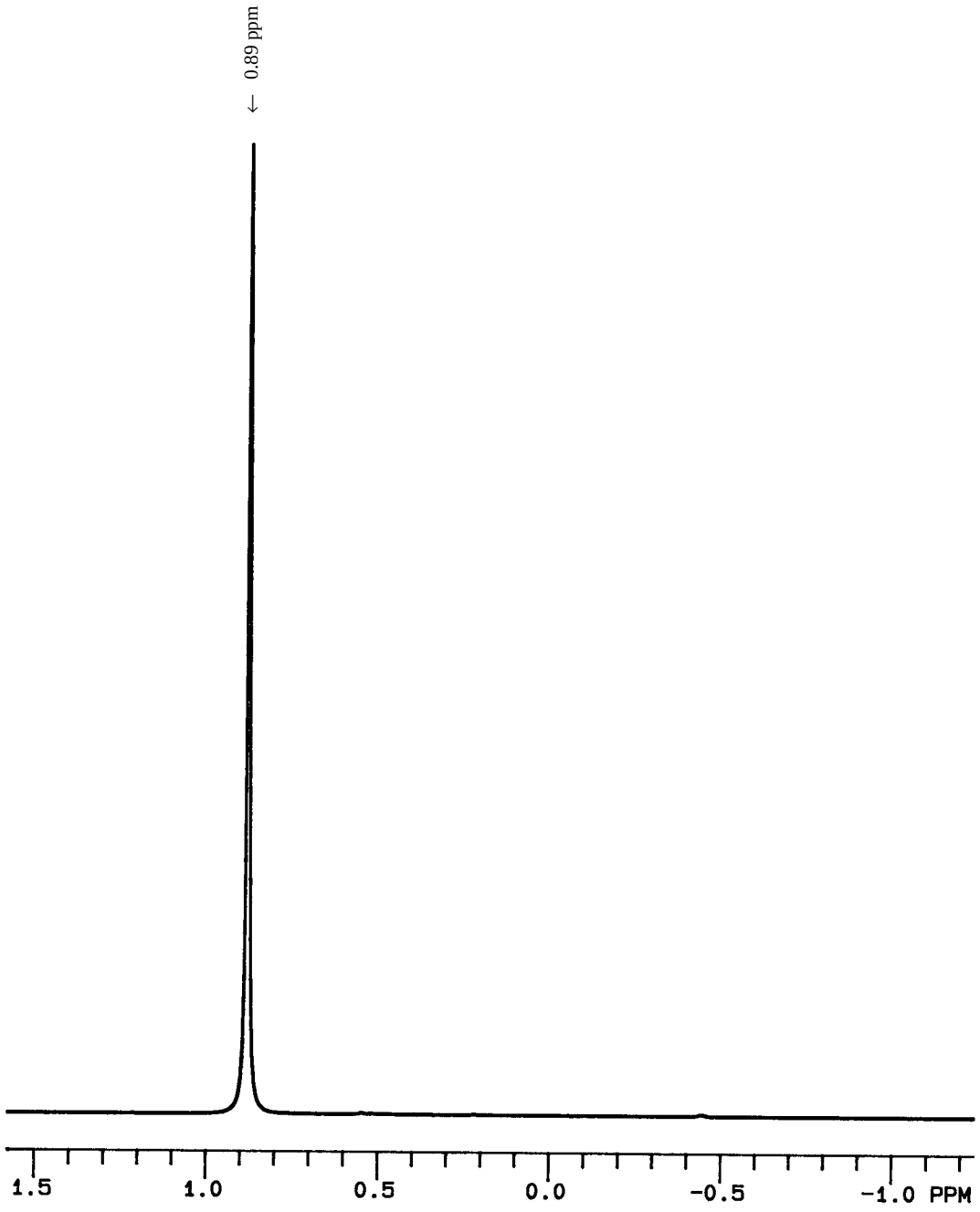


Figure 3 – ^{6}Li NMR spectrum of 2-ethyl-1-butyllithium at room temperature.

The ^{13}C NMR spectra show the same 5 peaks at all temperatures. The peaks for carbons c2, c3 and c4 shift somewhat upfield or downfield but no drastic changes are observed. However, the alpha carbon (c1) peak changes significantly. Figure 4 shows an expansion of the alpha carbon peak at different temperatures. As the temperature is first dropped to 14.4 °C, the broad peak starts to show some multiplet resolution. Lowering the temperature further, the resolution of the multiplet keeps getting better and the peak shifts upfield. At – 10.4 °C, the multiplet reaches its best resolution and the coupling measured is 3.19 Hz, which is the distance between adjacent lines in the multiplet. This coupling magnitude is consistent with a fluxional hexameric aggregate according to the range of couplings (3.1~3.4 Hz) observed for other hexameric alkyllithium compounds.[4] The experimental formula presented in Chapter I ($J_{13C\text{-}6Li} = 17 \pm 2$ Hz / n) gives n = 5.33 for this coupling, but no aggregates are known to have an aggregation state equal 5. This is the experimentally observed coupling between the alpha carbon from the alkyl group and all six ^{6}Li nuclei in the aggregate because, even though the interaggregate exchange process has been hindered, the intraaggregate exchanges are making the alkyl groups move around the aggregate. This is called a fluxional hexamer.

In addition to the evaluation of the magnitude of the coupling between ^{13}C and ^{6}Li nuclei, another method can be applied to determine the aggregation state of the 2-ethyl-1-butyllithium. Because the alpha carbon multiplet showed good resolution at – 10.4 °C, it is suitable for a line shape analysis. This method consists of comparing the intensity of the lines in the observed multiplet with various simulated multiplets, which are designed to represent multiplets of compounds with different aggregation states. Each simulated

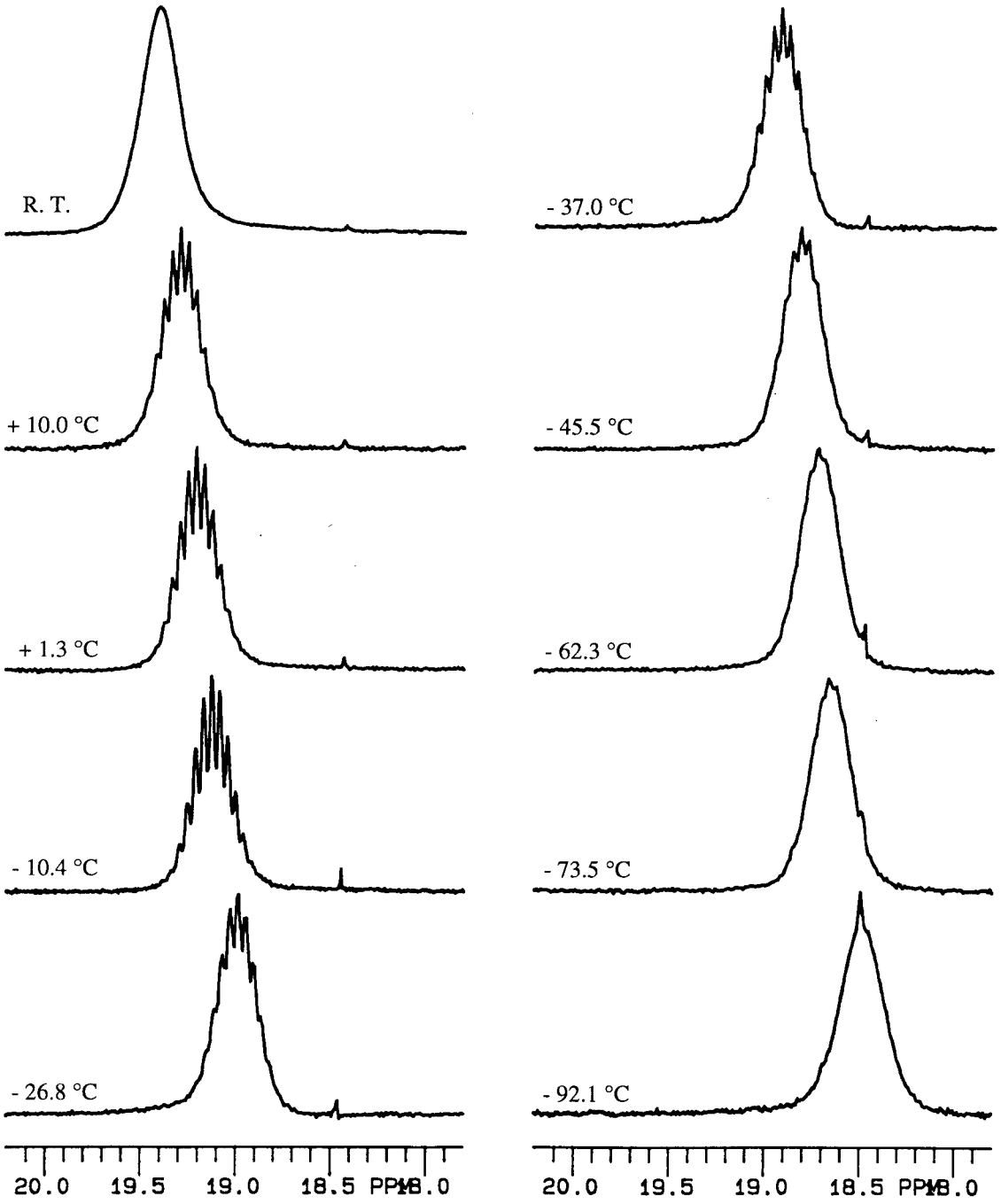


Figure 4 – ^{13}C NMR spectra of the alpha carbon region of 2-ethyl-1-butyllithium at different temperatures.

multiplet has a different aggregation state so that the total number of ^{6}Li nuclei that the alpha carbon would be coupled to is different. Consequently, the multiplets have different numbers of lines, and the lines in those multiplets have different relative intensities.

These multiplets are simulated using information from the observed multiplet such as the coupling constant and the line width of the lines in order to get a good fit. With aggregates larger than hexamers, it becomes harder to identify all the lines in a multiplet due to the very low intensity of the outside lines compared to the lines in the center of the multiplet. Therefore, a fluxional nonamer aggregate, which, for example, should have a nineteen-line multiplet, may not present all these lines in its alpha carbon multiplet. This may cause confusion because an octamer may also present fewer lines in its multiplet despite the fact it should have seventeen lines, and look very much alike the nonamer's multiplet. Even if multiplets seem to have the same multiplicity, the simulation will differentiate them by the intensity of the lines.

Multiplet simulations were made using a computer program written by Nguyen[6] for aggregation states n = 2, 3, 4, 5, 6, 7, 8 and 9. This program uses experimental data from the ^{13}C NMR spectrum to be analyzed, but the number of lithium nuclei can be varied to simulate different aggregation states. The parameters used for these simulations were the observed field strength of 75.43 MHz, the experimental chemical shift of 19.13 ppm, coupling constant of 3.19 Hz, and linewidth of 2 Hz. The linewidth was selected within the range from the smallest to the largest linewidth observed for the peak in the spectrum to give the best approximantion. The simulation with the best fit was the hexamer that is shown in Figure 5. The other simulations were

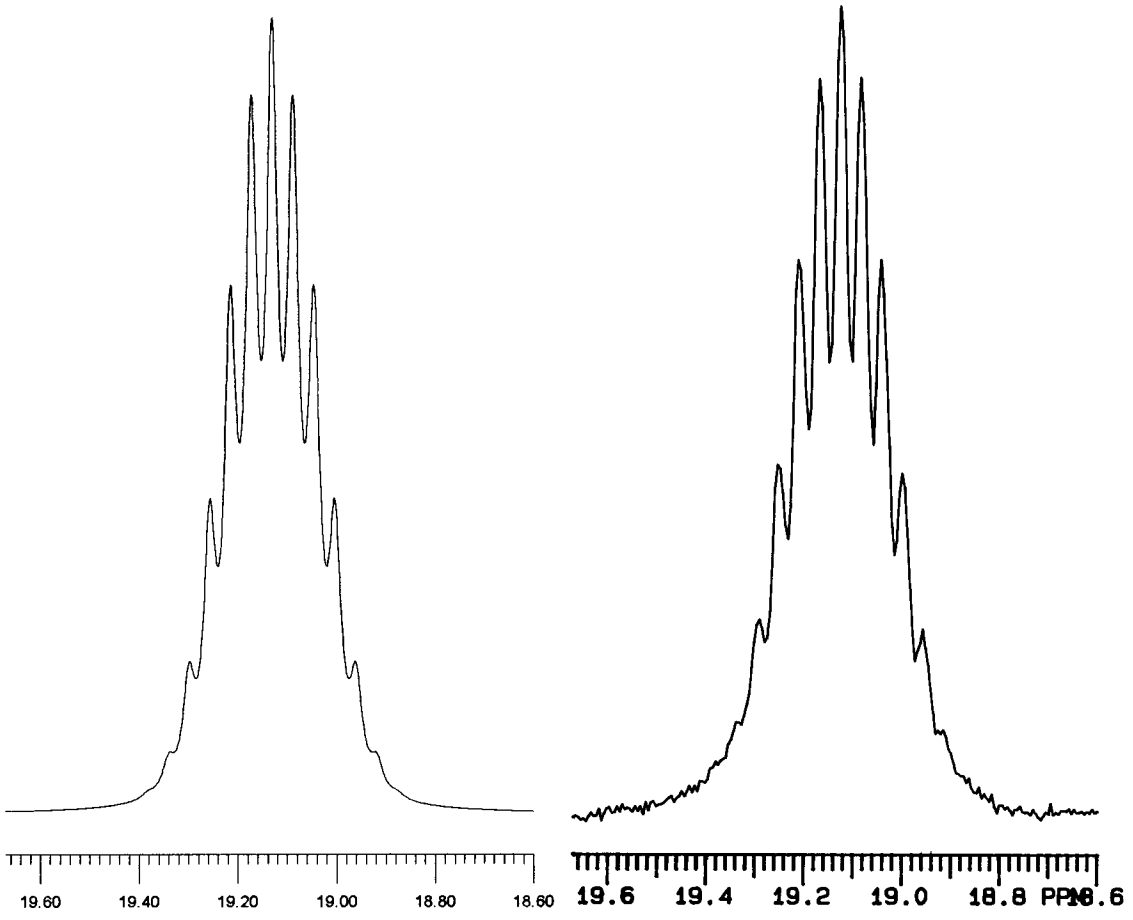


Figure 5 – Simulation (left) and experimental (right) ^{13}C NMR spectrum of the alpha carbon region of the 2-ethyl-1-butyllithium at – 10.4 °C.

discarded because they did not match the peak intensities of the observed multiplet. This is unambiguous evidence for the assignment of 2-ethyl-1-butylliythium as a hexameric aggregate.

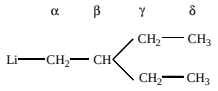
Another change is observed in the alpha carbon peak as the temperature continues to drop. The multiplet loses its resolution and becomes a broad peak again. This means that it was not possible to stop the intraaggregate exchanges in this temperature range studied. If stopping the interaaggregate exchange were possible, a different multiplet would be observed. This multiplet would have different coupling and multiplicity. A non-fluxional hexamer aggregate would have each alpha carbon coupled to only three ^{6}Li nuclei and, therefore, it would be a five-line multiplet. However, a hexamer aggregate has two open triangular faces that may favor the fluxionality, making it difficult to stop such intraaggregate exchange process.

All different low temperature ^{6}Li NMR spectra show only the one peak that was observed at room temperature. The peak shifts slightly upfield as the temperature is decreased. At – 16.3 °C, close to the temperature where the ^{13}C multiplet showed the best resolution, the ^{6}Li spectrum shows very clearly two ^{13}C satellites at the base of the singlet. These satellites started appearing around – 0.4 °C, and the distance between them is 3.1 Hz, which is the same coupling that had been measured in the ^{13}C NMR spectrum.

All these low temperature data indicate clearly that only one aggregate is present at all temperatures of this study. This is a different result from what was observed for straight chain alkyl groups. The straight chain alkyllithium compounds were observed to form different and larger aggregates in hydrocarbon solvents at low temperatures.[5]

Therefore, the addition of a branch at the beta carbon of the alkyl group has been effective in adding enough steric bulk to hinder the formation of larger aggregates.

Table 3 – Summary of NMR spectral data for 2-ethyl-1-butyllithium.

2-Ethyl-1-butyllithium 	
^{1}H NMR spectrum * estimate	α = - 0.83 ppm; doublet; $J_{H\alpha\text{-}H\beta}$ = 6.8 Hz β = 1.06 ppm; multiplet; $J_{H\beta\text{-}H\alpha}$ = 6.8 Hz; $J_{H\beta\text{-}H\gamma}$ = 5.8 Hz γ' = 1.31 ppm*; multiplet; $J_{H\gamma'\text{-}H\beta}$ = 5.8 Hz*; $J_{H\gamma'\text{-}H\delta}$ = 7.3 Hz γ'' = 1.39 ppm*; multiplet; $J_{H\gamma''\text{-}H\beta}$ = 6.4 Hz*; $J_{H\gamma''\text{-}H\delta}$ = 7.3 Hz δ = 0.89 ppm; triplet; $J_{H\delta\text{-}H\gamma}$ = 7.3 Hz;
^{13}C {^{1}H} NMR spectrum	α = 19.39 ppm; broad singlet at room temperarute; at – 10.4 °C, 19.13 ppm; multiplet ($J_{13C\text{-}6Li}$ = 3.19 Hz) β = 42.21 ppm γ = 31.59 ppm δ = 10.87 ppm
^{6}Li {^{1}H} NMR spectrum	Single peak at 0.89 ppm, slightly shifting upfield with decrease in temperature; At – 16.3 °C, ^{13}C satellites are observed ($J_{13C\text{-}6Li}$ = 3.1 Hz)
Aggregation state	Hexamer (only one aggregate observed at all temperatures)

<u>2-Ethyl-1-butyllithium/lithium 2-ethyl-1-butoxide</u>

Four samples were prepared mixing the alkyllithium, 2-ethyl-1-butyllithum, and the alcohol, 2-ethyl-1-butanol, as described in Chapter II. The preparation of these samples involves the reaction between the alkyllithium and the alcohol to form the lithium alkoxide and the alkane, as a byproduct. The first two samples that will be

discussed are the 0.2 and 0.4 oxygen to lithium ratio (O:Li = 0.2 and 0.4). These samples are considered to have low O:Li ratios, and they should favor the formation of mixed aggregates richer in alkyl groups rather than alkoxides. At low ratios, more alkyl groups will be available in solution than alkoxides, favoring these alkyl rich mixed aggregates. The other two samples have higher ratios (O:Li = 0.6 and 1) and different mixed aggregates are expected, possibly richer in alkoxide groups because more alkoxide groups will have formed and less alkyl groups will remain unreacted.

The other samples that will be discussed did not involve an *in situ* synthesis. One of these samples is the lithium 2-ethyl-1-butoxide, which was synthesized independently from the alkyllithium. This sample's spectra will be used as a standard to verify the presence of exclusive lithium alkoxide aggregates among the mixed aggregates that are expected to form in all the other samples. The other sample used this lithium 2-ethyl-1-butoxide to make a simple mixture of alkyllithium and lithium alkoxide. There is no alkane left in this sample because no reaction took place. This sample's purpose is to investigate whether or not this alternative sample preparation would also give mixed aggregates.

O:Li = 0.2 and 0.4

The sample with O:Li ratio of 0.2 was analyzed by ^{1}H, ^{13}C and ^{6}Li NMR spectroscopy in the temperature range of room temperature to – 95.3 °C. However, the low temperatures analyses will be concentrated on those spectra obtained at temperatures around – 10 °C, which is the temperature range in which the interaggregate exchange

processes are slower as was observed for the pure 2-ethyl-1-butyllithium sample. For the mixed samples, this temperature is also interesting because it was observed the appearance of major peaks in the spectra analyzed in this study, indicating the formation of mixed aggregates.

Figure 6 shows the ^{1}H NMR spectrum of this sample at room temperature. This spectrum certainly looks different from the spectrum of the pure alkyllithium sample. The first thing to be noticed is the appearance of new peaks in the spectrum. The region where the alkyl alpha protons were observed for the alkyllithium at around – 0.85 ppm now shows a very broad peak. This broad peak is likely to be the overlap of different doublet peaks from magnetically different alkyl groups. The presence of new peaks confirms the expectation of new aggregates forming in solution after the reaction of the alkyllithium with alcohol. There is also the appearance of new peaks in a region where no peaks had been observed before for the alkyllithium sample. This region is around 3.50 ppm. Two doublet peaks can be observed at 3.56 and 3.40 ppm, at room temperature.

Considering that these new peaks must be from the alkoxide groups that were formed, the peaks must also be the alkoxide alpha protons because they are the only protons in the alkoxide group that would give a doublet. The proton peaks splitting pattern of the alkoxide group is identical to the alkyl group that was discussed earlier. The alpha protons give a doublet, the beta and gamma protons give multiplets, and the delta protons in the methyl end give a triplet. Therefore, the alkoxide alpha protons have a very distinct region where they appear in the ^{1}H NMR spectrum and can be clearly

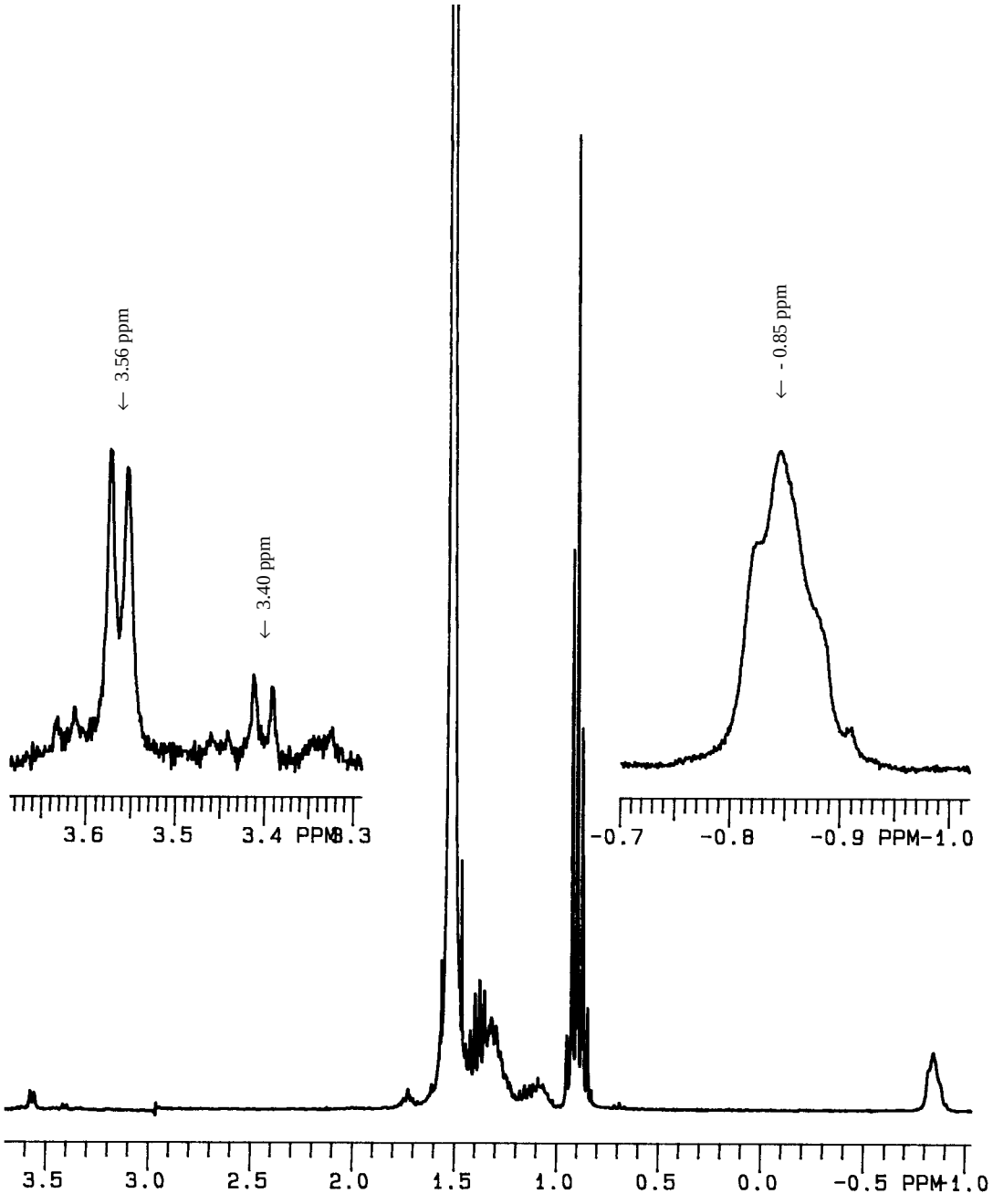


Figure 6 – ^{1}H NMR spectrum of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.2 at room temperature. Insets show the expansion of the alkoxide alpha proton region (left) and the alkyl alpha proton region (right).

observed. The other peaks have their chemical shifts close to the peaks in the alkyl groups and can not be assigned properly due to the overlap of the peaks.

Because the alkyl alpha protons and alkoxide alpha protons are in such different regions in the spectrum, and they are not overlapping with different types of protons, the integration of the peaks in these two different regions should be representative of the amount of these two groups of protons. So, the integration ratio between the two regions must correspond to the ratio between alkyl and alkoxide groups. The integration of this spectrum at room temperature in the alkoxide alpha proton region is equivalent to 18.35% and the alkyl alpha proton is 81.65%. The O:Li ratio calculated from the integration values obtained is 0.18, which is close to the ratio of 0.2 intended for this sample.

Upon lowering the temperature, the ^{1}H NMR spectrum starts changing. The broad peak in the alkyl alpha proton region begins to resolve into doublet peaks at 5.1 °C. Even though these peaks are still overlapping, at least three doublet peaks can be identified at – 0.84, – 0.88 and – 0.91 ppm as is shown in Figure 7 at – 12.3 °C. The doublet at – 0.84 ppm is the same observed for the pure alkyllithium, and it has a higher intensity than the other doublets, which indicate that the original aggregate is still present in solution and in a large amount. The peaks in the alkoxide alpha proton region also change with lower temperatures. In contrast to the spectrum at room temperature where one doublet at 3.56 ppm was more pronounced than the others, three doublets are present with similar intensities at – 12.3 °C, in Figure 7. In addition to the doublet at 3.56 ppm, the other two doublets at 3.38 and 3.31 ppm seemed to have grown in intensity at this lower temperature. The 3.38 ppm peak is probably the 3.40 ppm observed at room temperature

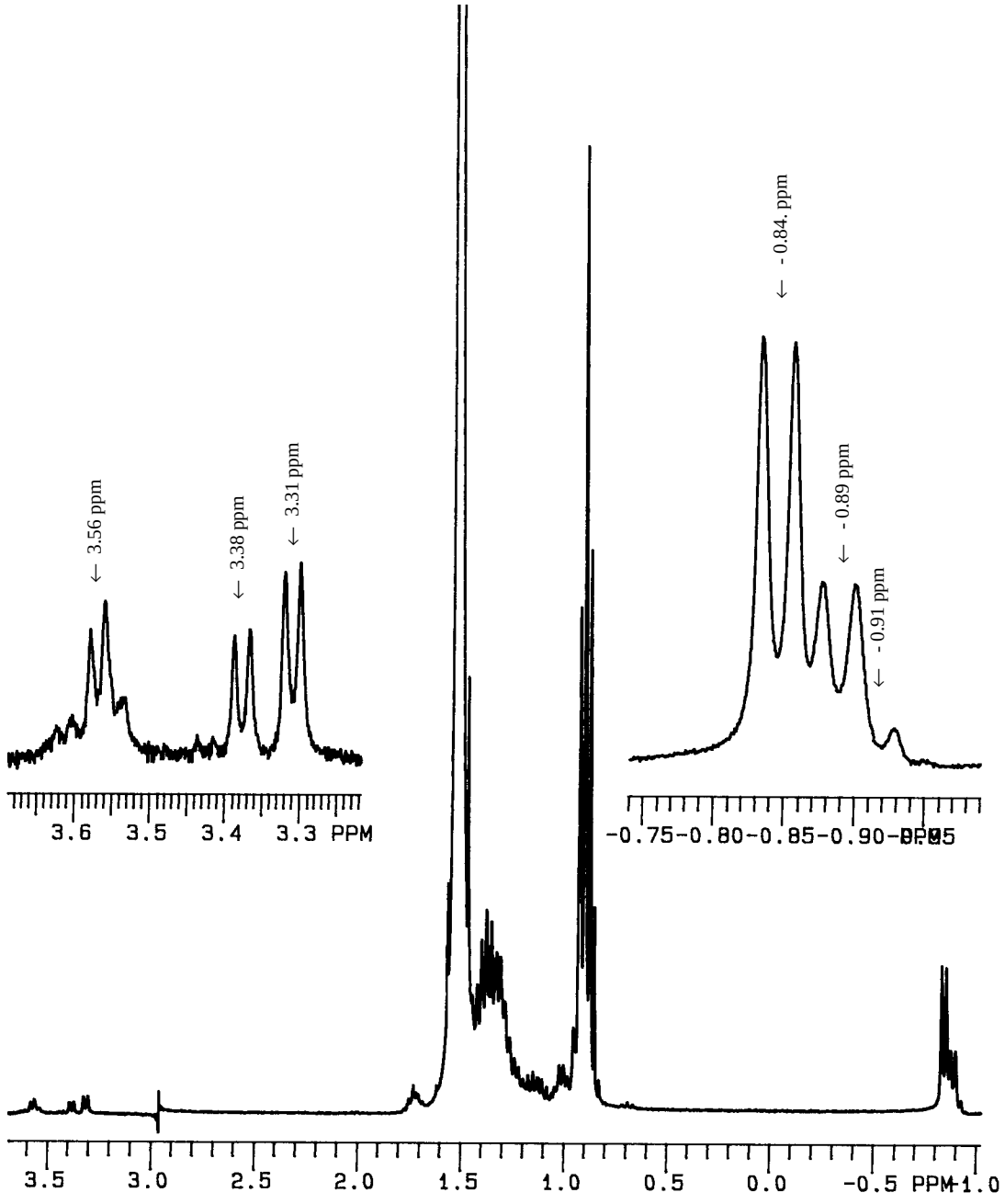


Figure 7 – ^{1}H NMR spectrum of a mixture of 2-ethyl-1-butlyllithium and 2-ethyl-1-butanol with O:Li = 0.2 at – 12.3 °C. Insets show the expansion of the alkoxide alpha proton region (left) and the alkyl alpha proton region (right).

that have shifted upfield, and the 3.31 peak is a new peak that has now appeared. This indicates the presence of three magnetically different alkoxide groups that could correspond to three different new aggregates. The data presented so far point to the presence of four aggregates in solution, the original alkyllithium and three new alkyllithium/lithium alkoxide aggregates at – 12.3 °C. However, more data needed to be analyzed. The changes observed in the spectra show that the distribution of aggregates varies with temperature.

Upon continued lowering of the temperature, the relative intensities of the doublets keep varying and the resolution of these peaks decreases. At temperatures below – 77 °C, the downfield peaks at around 3.50 ppm seem to be buried in the base line and the upfield peaks become a single broad peak. These changes are probably due to some of the aggregates falling out of the solution with the temperature drop.

The ^{13}C NMR spectrum of this sample at room temperature is shown in Figure 8. This spectrum has many more peaks than the spectrum of just the alkyllithium. The major peaks observed are at 66.30, 47.59, 42.28, 36.42, 31.66, 29.26, 25.89, 23.66, 19.38, 18.41 and 10.92 ppm. These peaks are from the 2-ethyl-1-butyllithium, lithium 2-ethyl-1-butoxide, 3-methyl pentane and also the solvent cyclopentane. The peak at 25.89 ppm is from the solvent, cyclopentane, and it was used to reference the spectrum. The peaks at 42.28, 31.66, 19.38 and 10.92 ppm have practically the same chemical shifts of the beta, gamma, alpha and delta carbons of the alkyllithium, respectively. This can be interpreted as the peaks of the exclusive alkyllithium hexameric aggregate that is still present in solution. By comparison and with data from an Attached Proton Test (APT) spectrum,

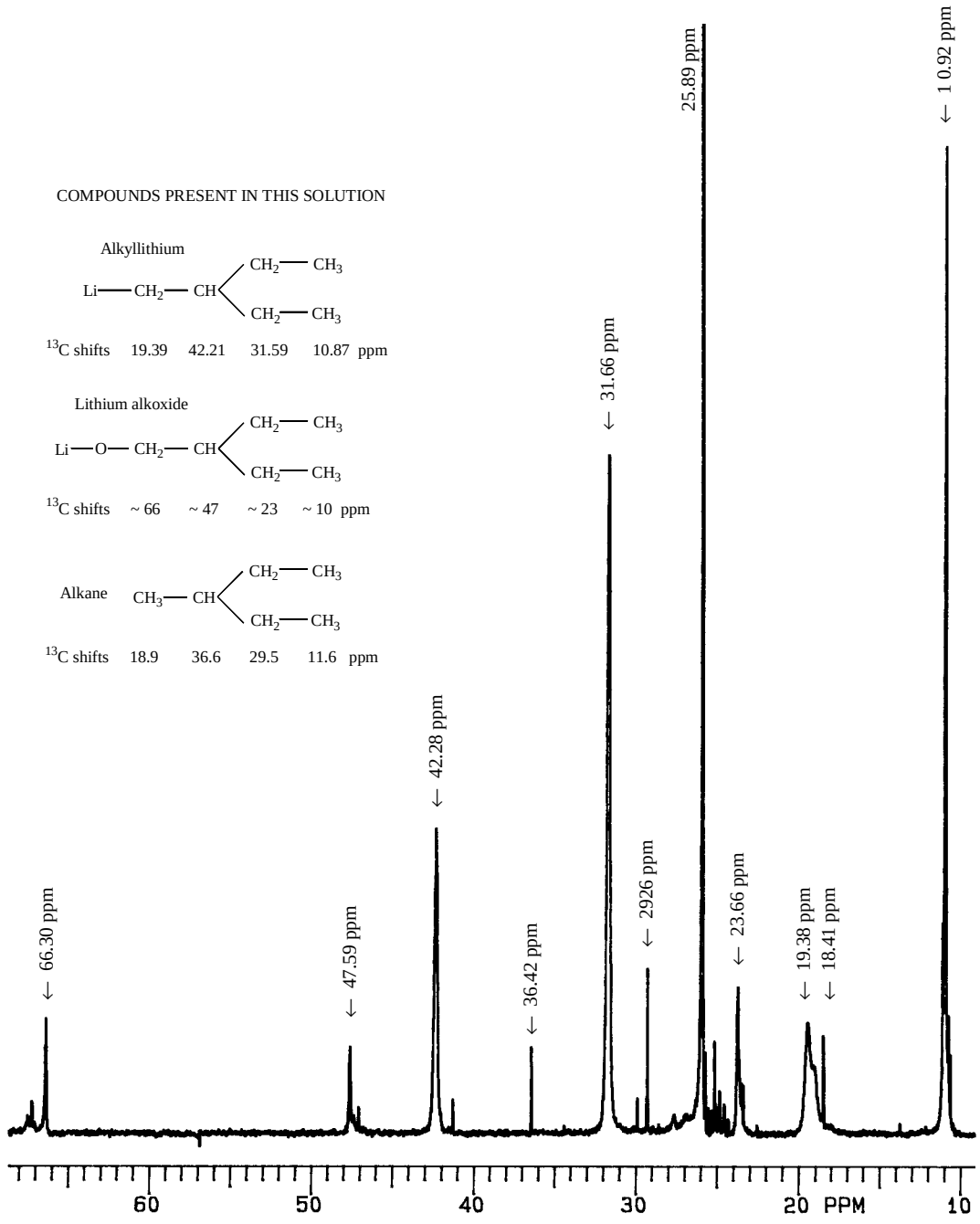


Figure 8 – ^{13}C NMR spectrum of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.2 at room temperature. Inset shows the compounds present and their chemical shift assignments.

the new peaks at 66.30, 47.59, 23.66 are assigned to the alpha, beta and gamma carbons of the lithium alkoxide, respectively. The peak for the alkoxide's delta carbon must be overlapping with the delta carbon's peak from the alkyllithium at 10.92 ppm.

The alkane formed from the reaction between the alkyllithium and the alcohol is the 3-methyl pentane, whose ^{13}C chemical shifts are 36.6, 29.5, 18.9 and 11.6 ppm.[7] The peaks observed at 36.42, 29.26 and 18.41 ppm are from the carbons 3, 2 and 4, and the methyl branch of the 3-methyl pentane. The peak for carbons 1 and 5 of this alkane must also be overlaping with the delta carbon's peak of the alkyllithium.

Some smaller peaks can be observed around the peaks at 66.30, 42.31, 23.66 and 10.92 ppm that are assigned as the same type of carbon but in a different aggregate. This is evidence for the possibility of having multiple aggregates in solution, which explains these slightly different chemical shifts. The peaks at 42.28 and 31.66 ppm are slightly broader than the other peaks, probably because they are also overlapping with other smaller peaks.

Given these assignments, two different regions can be defined. These regions are the alkyl alpha carbon region around 19 ppm and the alkoxide alpha carbon region around 66 ppm. In the alkyl alpha carbon region, a very broad peak is observed at 19.38 ppm and is exclusive by the alkyllithium aggregate. However, a shoulder can be observed to the right of this peak, which is evidence for the formation of at least one mixed aggregate, because this shoulder must be an overlapping peak from a new alkyl alpha carbon in a different aggregate.

The ^{13}C NMR spectrum starts showing changes with decreasing temperature in the same way observed for the ^{1}H NMR spectrum. The broad alkyl alpha carbon peak begins to resolve into three different peaks, but they are still broad due to the coupling to the ^{6}Li nuclei. The peaks at 42, 31 and 10 ppm become narrower and smaller peaks can be observed on their sides. Small peaks observed around the peaks at 66 and 47 ppm at room temperature begin to increase in intensity as the temperature decreases. Also, most peaks in the spectrum shift upfield with the decrease in temperature.

These changes can be seen in Figure 9, that shows the ^{13}C NMR spectrum of this sample at – 9.0 °C. At this temperature, the alkyl alpha carbon at 19.09 ppm begins to show some multiplet resolution and the coupling observed is 3.1 Hz, which is the same coupling discussed earlier for the alkyllithium sample alone. The chemical shift at this temperature also matches the peak for the alkyllithium aggregate. Therefore, this spectrum confirms the presence of hexameric alkyllithium, in addition to new mixed aggregates. At this temperature, two other broad peaks, 19.50 and 18.65 ppm, are observed in the alkyl alpha carbon region in addition to the sharp peak at 18.44 ppm from the alkane. However, other peaks may be present but not be observed due to broadness of these peaks and overlapping peaks.

The alkoxide alpha carbon region shows three major peaks at 67.09, 66.99 and 66.07 ppm that are probably from alkoxide groups in mixed aggregates. Considering that these alkoxide groups are possibly in different aggregates and no exclusive lithium alkoxide aggregate is present in this solution, the spectral data are consistent with the formation of three major alkyllithium/lithium alkoxide mixed aggregates at this

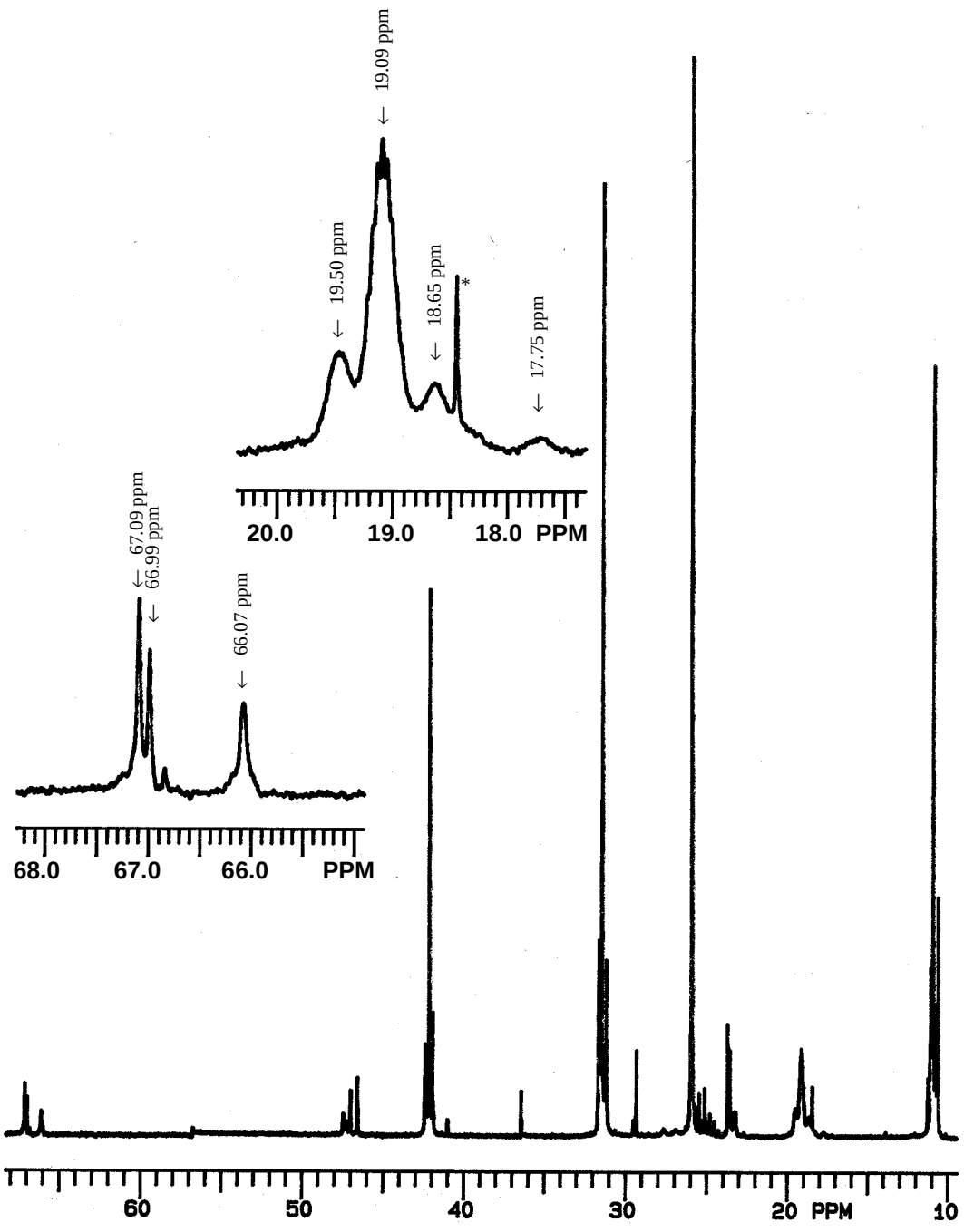


Figure 9 – ^{13}C NMR spectrum of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.2 at – 9.0 °C. Insets show the expansion of the alkoxide alpha carbon region (lower left) and the alkyl alpha carbon region (upper left). Asterisk indicates an alkane peak (18.44 ppm).

temperature. The study of the sample continues with more NMR experiments looking for more evidence for these mixed aggregates and more information to help characterize them.

As observed for the ^{1}H NMR spectra, the ^{13}C NMR spectra showed better resolution with a drop in the temperature. Nevertheless, the low temperature ^{13}C NMR spectra series also showed that further decrease in temperature led to the decrease of intensity in the peaks around the alkoxide alpha carbon region. This observation is consistent with previous results showed in the ^{1}H NMR spectra, indicating that the alkoxide groups tend to fall out of the solution at very low temperatures.

The ^{6}Li-enriched NMR spectroscopy of the mixed samples can give helpful information in the analyses of the mixed aggregates in solution and complement the analyses of ^{1}H and ^{13}C NMR spectra. The ^{6}Li NMR spectrum at room temperature for the sample with O:Li = 0.2 is shown in Figure 10. There are two very broad peaks overlapping, 0.82 and 0.48 ppm, and they are most likely exchanging magnetization in a dynamic process. This is supported by the broadness of these peaks and that rapid intra and interaggregate exchange processes are known to take place on the ^{13}C NMR time scale at room temperature. The exchange between two peaks makes them shift towards each other. Therefore, the most downfield of them must correspond to the alkyllithium aggregate, which is shifted upfield from 0.89 to 0.82 ppm. These data show that the alkyllithium aggregate is still present in this solution even though it is exchanging with a mixed aggregate.

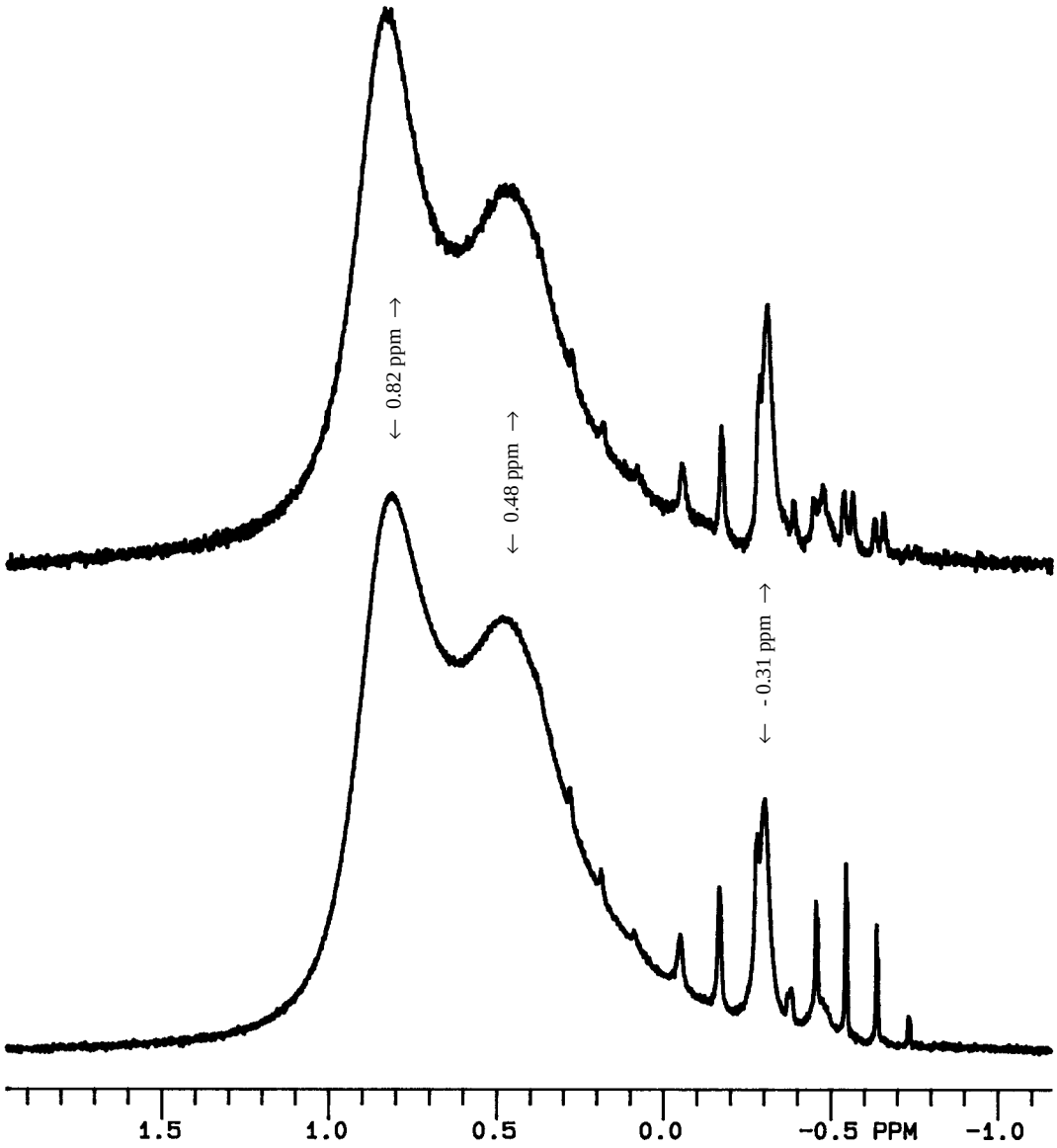


Figure 10 – ^{6}Li NMR spectra of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.2 at room temperature with ^{1}H decoupling (bottom) and without (top).

Generally, each peak observed in the ^{6}Li NMR spectrum will correspond to a different aggregate, and, therefore, the second broad peak at 0.48 ppm likely represents a new and possibly mixed aggregate. The upfield peak at – 0.31 ppm is another important peak in this spectrum, because it should also be a new mixed aggregate formed in the solution. These data indicate the presence of possibly three aggregates in solution at room temperature, being the alkyllithium aggregate and two new alkyllithium/lithium alkoxide mixed aggregates. The other peaks present (- 0.05, - 0.17, - 0.45, - 0.54, - 0.64 and - 0.73 ppm) are very small in area when compared to the two broad peaks, and some of them (- 0.45, - 0.54, - 0.64 and - 0.73 ppm) split into doublets when the spectrum is run with the ^{1}H decoupler turned off. This clearly indicates that the lithium is coupled to one proton, which means that the aggregate associated with that peak has a hydride in place of an alkyl group.

The presence of hydrides in this sample can be explained as being a consequence of the method used in preparing the samples. The reaction that occurs when the alcohol is added to the alkyllithium solution is extremely exothermic and, therefore, produces enough heat even to evaporate some of the solvent. If too much heat is generated at one time by the addition of a large amount of alcohol to the alkyllithium solution, this heat can induce beta-hydride elimination to form a lithium hydride/lithium alkoxide mixed aggregate. These types of aggregates have been reported in the literature and found to be very strong bases with only one hydride ion per aggregate.[8] The beta-hydride elimination can also be induced photochemically as well as thermally. Therefore, to reduce the exposure of the samples to light and heat, the NMR tubes were always covered with

aluminum foil and kept in the refrigerator while they were not being analyzed. Keeping the samples in these conditions prevents them from deteriorating too fast and also maintains the amount of hydrides to a minimum. The study of these lithium hydride/lithium alkoxide mixed aggregates is not the focus of this thesis, but it is certainly a topic for future investigations.

Lowering the temperature should also promote changes in the ^{6}Li NMR spectrum, as it did for the ^{1}H and ^{13}C NMR spectra. Figure 11 and Figure 12 show the ^{6}Li NMR spectra of this sample at + 5.1 °C and – 12.3 °C, respectively. As it has been argued, the decrease in temperature slows the interaggregate exchange processes, and it also favors the formation of larger aggregates in cyclopentane solution. These are the reasons for such drastic changes observed in these low temperature spectra. Slowing the interaggregate processes, the two downfield peaks become narrower and no longer overlap with each other (0.88 and 0.47 ppm) at 5.1°C (Figure 11). At – 12.3 °C, Figure 12, these peaks are even sharper. The second significant change observed is the appearance of one strong upfield peaks at – 0.12 in addition to the peak at – 0.30 ppm, which was observed at room temperature and has increased in intensity at low temperature. This new peak must correlate to a new mixed aggregate forming at low temperature, and the amounts of these mixed aggregates seem to be increasing with the decreasing temperature.

The peaks shift slightly upfield as the temperature decreases, and their chemical shifts at – 12.3 °C are 0.86, 0.47, - 0.14 and –0.32 ppm. There are still some other peaks observed at this temperature, but they are very small in intensity compared with the four

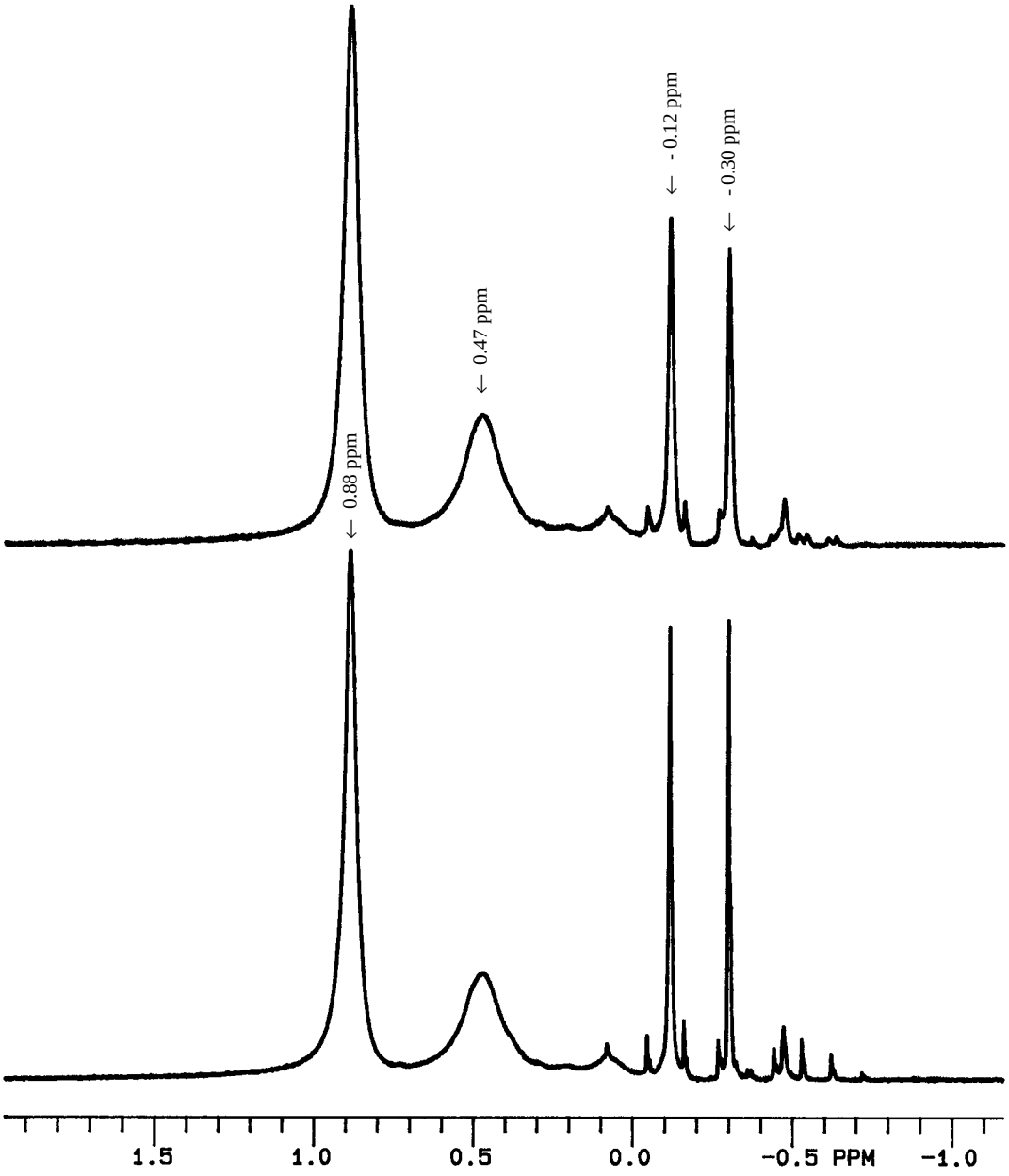


Figure 11 – ^{6}Li NMR spectra of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.2 at + 5.1 °C with ^{1}H decoupling (bottom) and without (top).

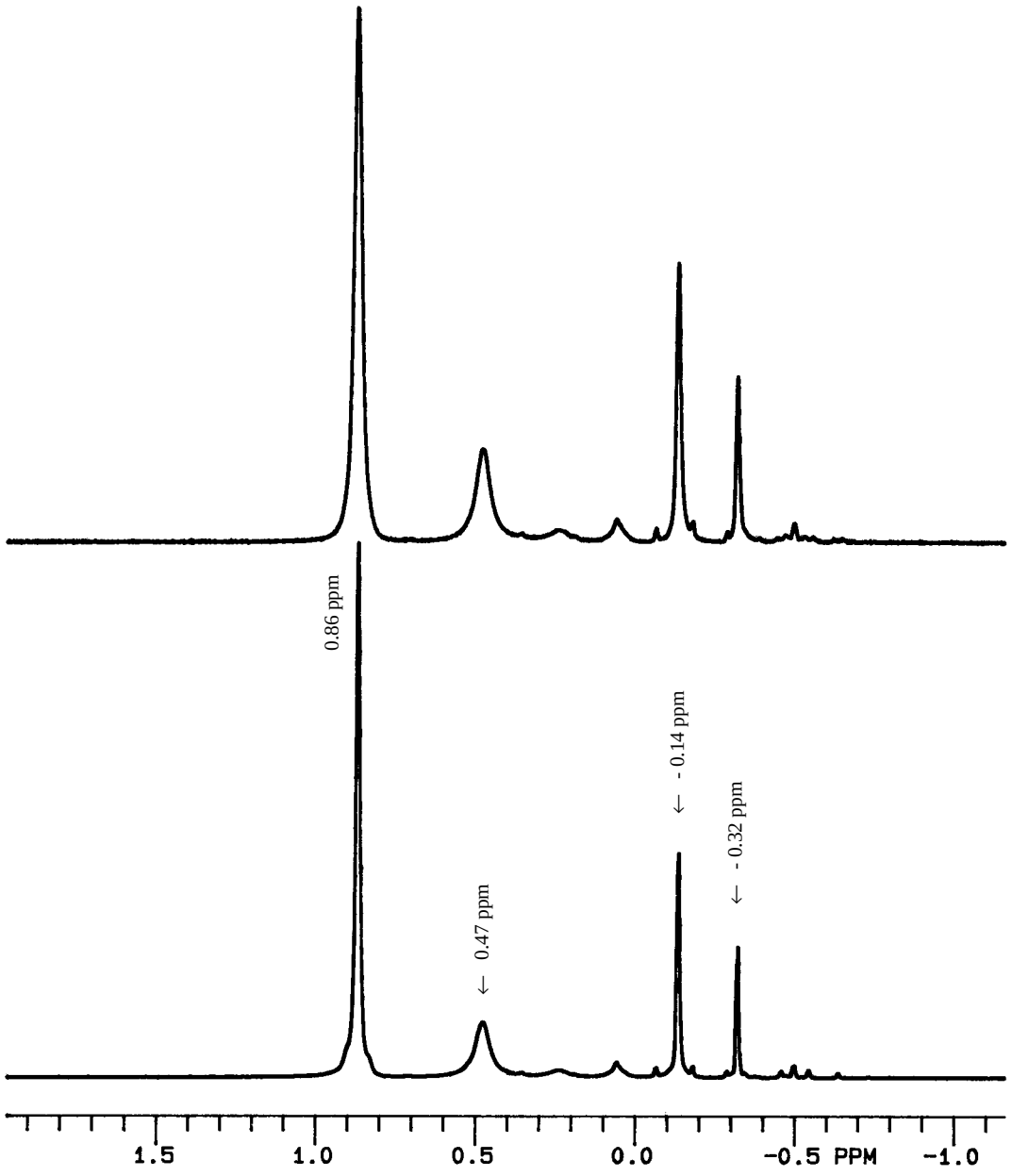


Figure 12 – ^{6}Li NMR spectra of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.2 at – 12.3 °C with ^{1}H decoupling (bottom) and without (top).

major peaks. Also, the peaks corresponding to aggregates with hydride became so small that they are almost buried in the base line. Due to the broad peaks at room temperature becoming narrow peaks at low temperature, the absolute intensities of these peaks have increased a lot at low temperature, giving the impression that some of the other peaks observed at room temperature have decreased in intensity. However, the intensity of the peaks is a relative measurement, and the integration of the peaks is the right parameter to indicate distribution amounts of the species in solution.

All the NMR data collected so far indicate the predominant presence of three aggregates at room temperature and four aggregates at low temperature, the alkyllithium aggregate and different alkyllithium/lithium alkoxide mixed aggregates. Although it is possible to differentiate the peaks between alkyl or alkoxide groups in the ^{1}H and ^{13}C NMR spectra, and to differentiate the ^{6}Li peaks related to the alkyllithium aggregate and the alkyllithium/lithium alkoxide mixed aggregates, the correlation between the alkyl and alkoxide peaks to the different aggregates is not clear. The correlation between peaks from different NMR spectra can be obtained in a two dimensional NMR spectrum (2D NMR), considering that transfer of magnetization occurs between the two nuclei involved in the experiment. For example, 2D ^{1}H-^{13}C HETCOR NMR, Heteronuclear Correlation NMR spectroscopy, could be used to show the correlation between the peaks of protons and carbons that are attached to each other in a given compound. However, in this case, determining the correlation between proton and carbon peaks that have already been assigned does not give any information about the mixed aggregates. A 2D ^{6}Li-^{13}C HETCOR NMR[9] spectra could be obtained, but it would not give the correlation between

the alkoxide groups and the lithium nuclei, because the oxygen atom between the carbon and the lithium prevents couplings between the ^{6}Li and ^{13}C nuclei.

The experiment used to get some useful information to help demonstrate the presence of the mixed aggregates was the 2D ^{1}H-^{6}Li HOESY[9] (Heteronuclear NOE Correlation Spectroscopy). This experiment gives the correlation between proton and lithium peaks, which are close to each other in the same aggregate. The proton and lithium nuclei are not directly bonded to each other in the aggregate, but the lithium nuclei can be affected by the proton nuclei close to them in space. This interaction can be used in a 2D NMR spectrum to show the correlation between the lithium nuclei and the alkyl or alkoxide alpha protons.

Figure 13 shows the 2D ^{1}H-^{6}Li HOESY spectrum of this sample at – 10.6 °C. This spectrum shows clear correlation between alkoxide alpha protons and the lithium peaks. The 3.31 ppm peak in the ^{1}H NMR spectrum is from a alkoxide alpha proton that is present in the aggregate with the lithium nuclei that appear at – 0.14 ppm in the ^{6}Li NMR spectrum, and the 3.38 ppm alkoxide alpha protons correlate to the – 0.32 ppm lithium nuclei. This spectrum did not plot a signal showing correlation between the lithium peak at 0.47 ppm and doublets in the alkoxide alpha proton region, but it does not necessarily mean that there is not one. Analyzing the traces of the 2D spectrum very carefully turn out to show correlation of that peak with the doublet at 3.56 ppm in the proton spectrum. The signal was not identified earlier because the 0.47 ppm peak is very broad and small, and its correlation could not be differentiated from the base line noise.

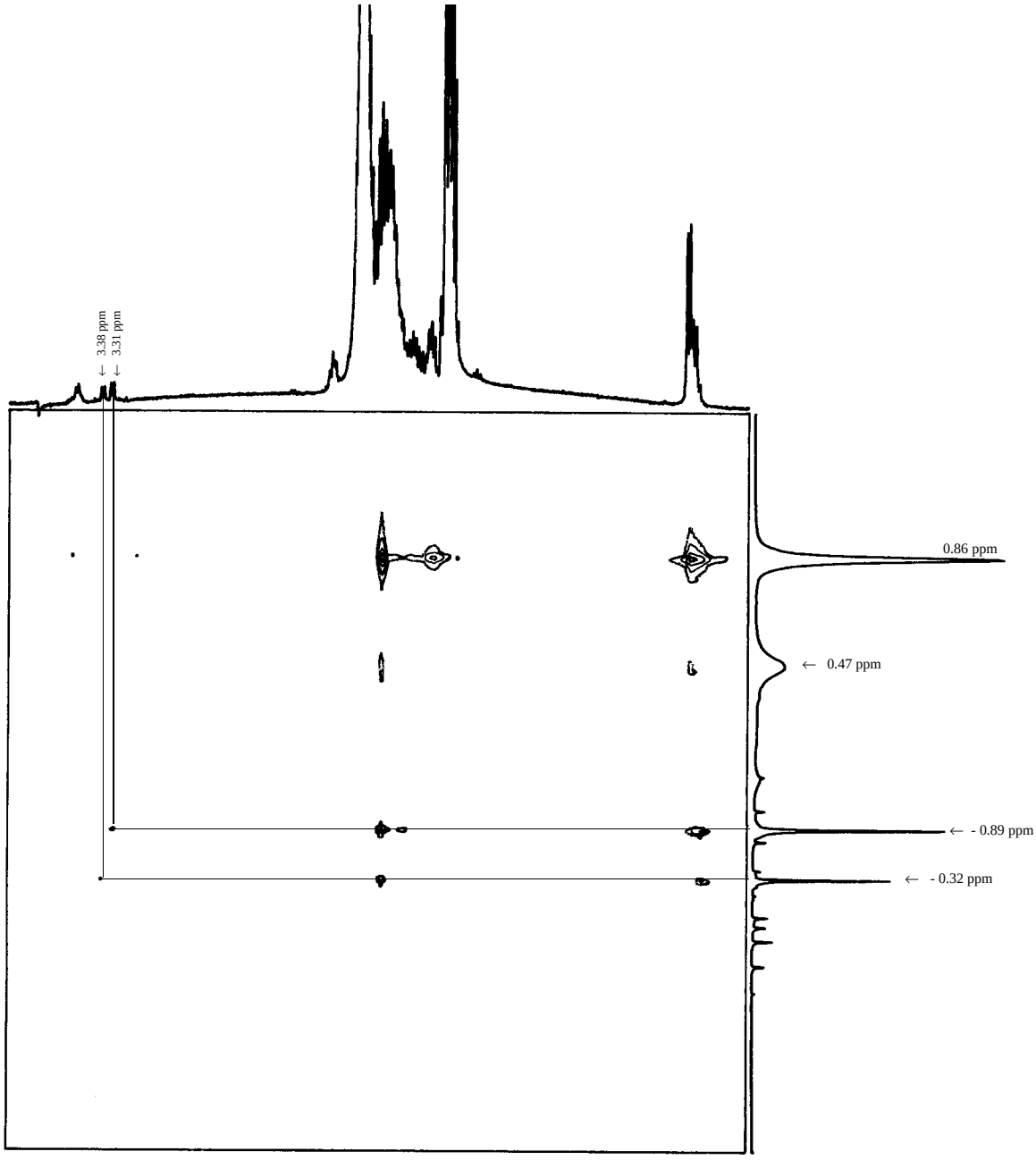


Figure 13 – ^{1}H-^{6}Li HOESY NMR spectrum of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.2 at – 10.6 °C.

This spectrum also shows clear correlation between the lithium nuclei and the alkyl alpha proton peaks, but an expansion is necessary to make the correlation assignments. The needed expansion of this spectrum is shown in Figure 14, and it shows that the four lithium peaks correlated to the peaks in the alkyl alpha proton region. The – 0.84 ppm proton doublet peak correlates to the 0.86 and 0.47 ppm lithium peaks, and the – 0.89 and – 0.91 ppm proton peaks correlates to the – 0.14 and – 0.32 ppm lithium peaks, respectively.

This is clear evidence that the mixed aggregates were formed in solution because both alkyl and alkoxide groups show simultaneous correlation to the same lithium peaks, and each lithium peak represents a different aggregate. The fact that the peak at 0.47 ppm shows correlation to the same alkyl alpha proton doublet as the peak at 0.86 ppm must be related to the dynamic exchange processes that still occur at this temperature. The interaggregate exchanges are still happening and the peak at 0.47 ppm is small and broad probably due to these exchanges.

Table 4 – Summary of NMR spectral data for 0.2 O:Li ratio sample at – 10.6 °C.

Alkyllithium/alcohol mixed sample with O:Li = 0.2 (at – 10.6 °C)					
Aggreg.	^{6}Li NMR shift	^{1}H NMR shift (alkyl alpha)	^{1}H NMR shift (alkoxide)	^{13}C NMR shift (alpha carbon)	Type
1	0.86 ppm	– 0.84 ppm	---------	19.09 ppm	Alkyllithium
2	0.47 ppm	– 0.84 ppm	3.56 ppm	---------	Mixed agg.
3	– 0.12 ppm	– 0.89 ppm	3.31 ppm	---------	Mixed agg.
4	– 0.32 ppm	– 0.91 ppm	3.38 ppm	---------	Mixed agg.

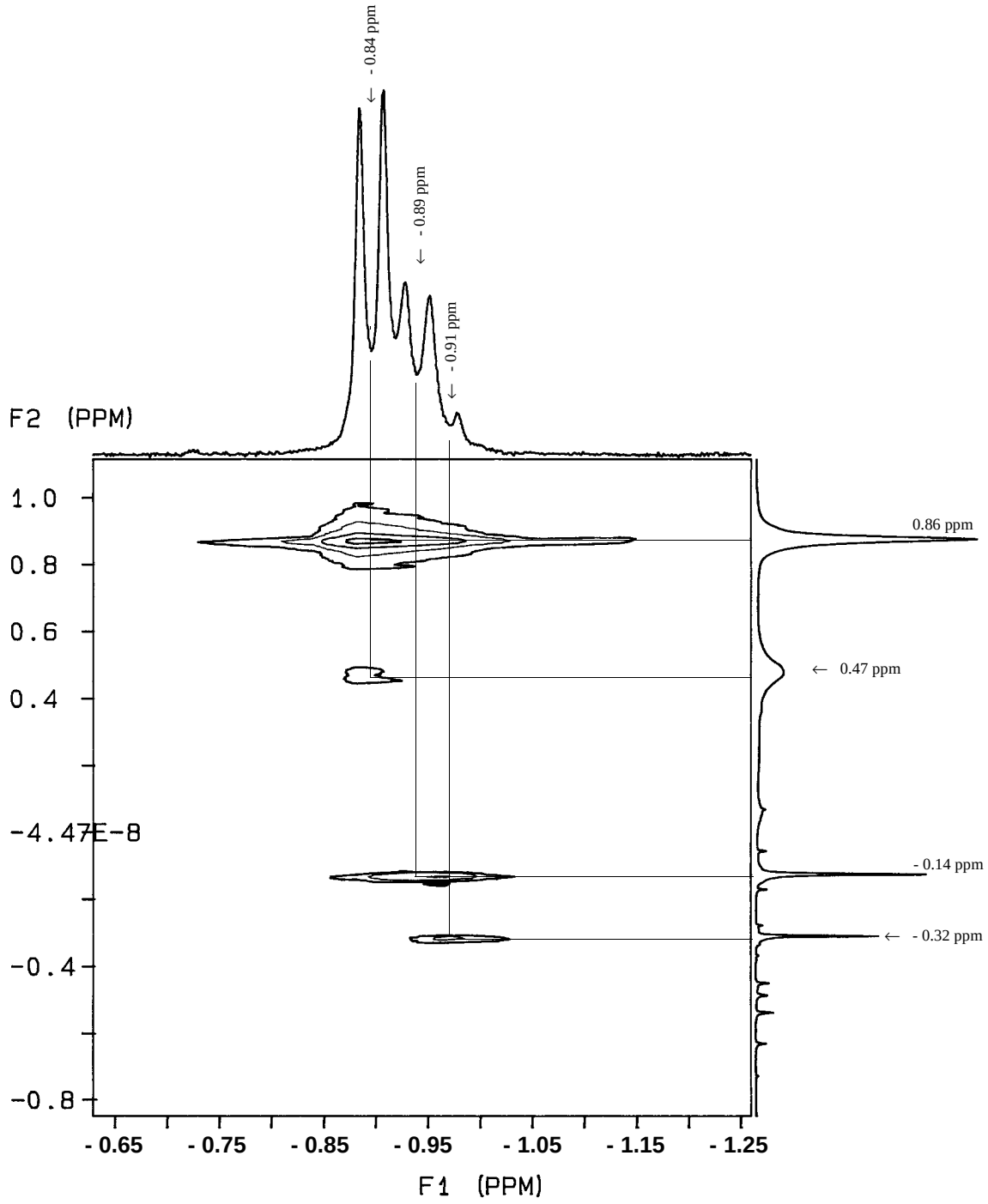


Figure 14 – Expansion of the alkyl alpha protons from ^{1}H-^{6}Li HOESY NMR spectrum of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.2 at – 10.6 °C.

The sample with O:Li = 0.4 showed approximately the same results as the 0.2 O:Li sample in the ^{1}H, ^{13}C ^{6}Li NMR spectra with respect to the peaks present and their chemical shifts. However, the intensity of the peaks changed, making possible the detection of new peaks at room temperature that had not been observed before. Furthermore, the differences in peak intensities indicate that the relative amounts of the different aggregates observed have also changed, which can be demonstrated by the integration of the peaks in the ^{6}Li NMR spectra. This sample also showed an increased amount of one mixed aggregate that was not considered before because its peaks were too small in comparison to the others in the ^{6}Li NMR spectrum.

Figures 15 and Figure16 show the ^{1}H NMR spectrum of this sample at room temperature and at – 11.7 °C. The integration of the alkyl and alkoxide alpha protons at room temperature shows that the calculated ratio of this sample is 0.36. This experimental ratio is close to the intended ratio of 0.4, and it is actually double the experimental ratio of 0.18 found in the 0.2 O:Li ratio sample. At room temperature, a very broad peak is observed in the alkyl alpha proton region at – 0.85 ppm. In the alkoxide alpha proton region, three doublets are observed at 3.56, 3.45 and 3.40 ppm. The doublet at 3.45 ppm is very small, and it was not detected in the sample with 0.2 O:Li ratio. This is evidence for the formation of a new aggregate in solution.

At lower temperature, Figure 16, the alkyl alpha proton peak is resolved into three doublets at – 0.84, – 0.89 and – 0.91 ppm, which are the same doublets observed for the O:Li = 0.2 sample at around the same temperature. These peaks are very close together and still overlapping, and they could be hiding other new doublet peaks that may

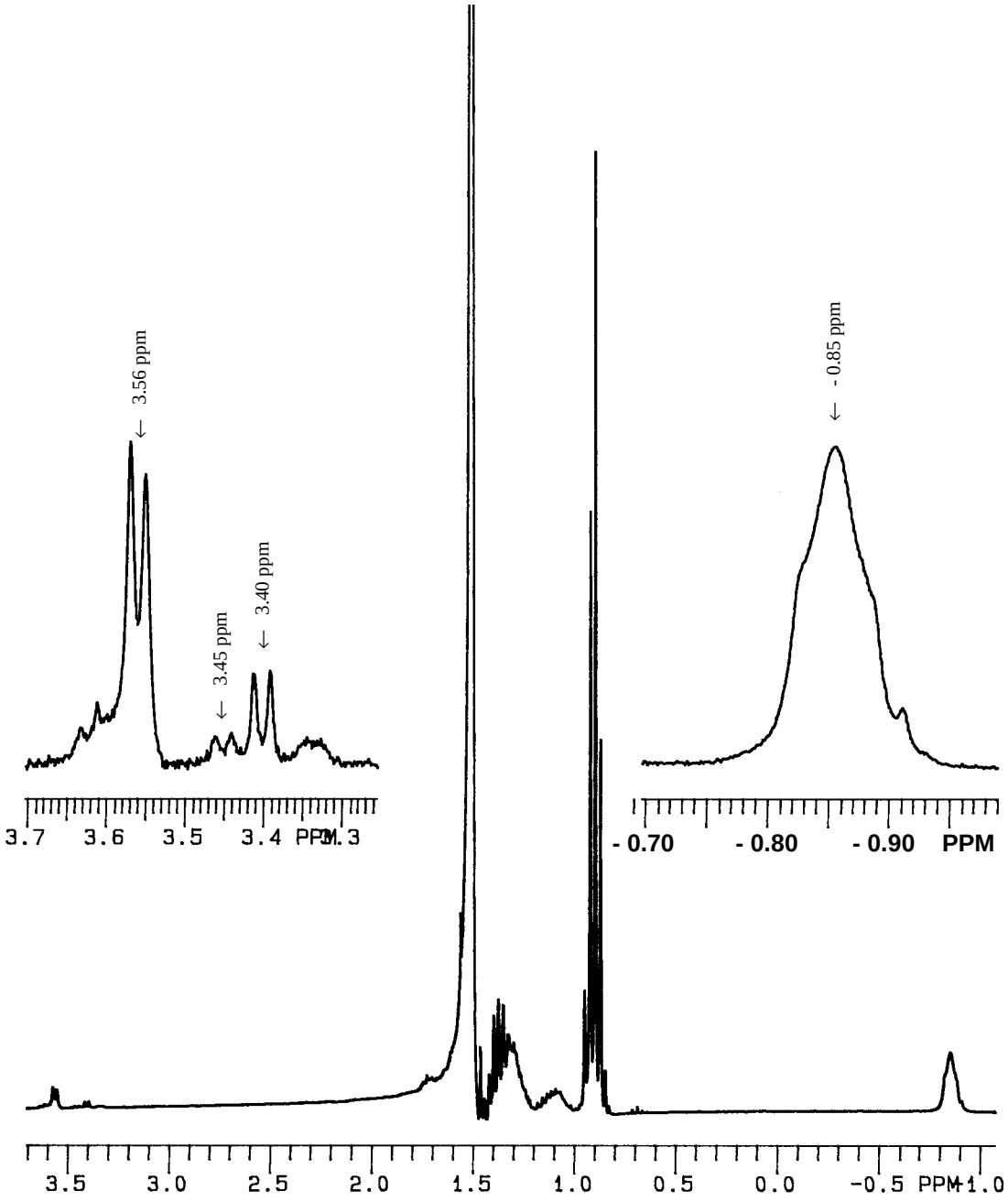


Figure 15 – ^{1}H NMR spectrum of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.4 at room temperature. Insets show the expansion of the alkoxide alpha proton region (left) and the alkyl alpha proton region (right).

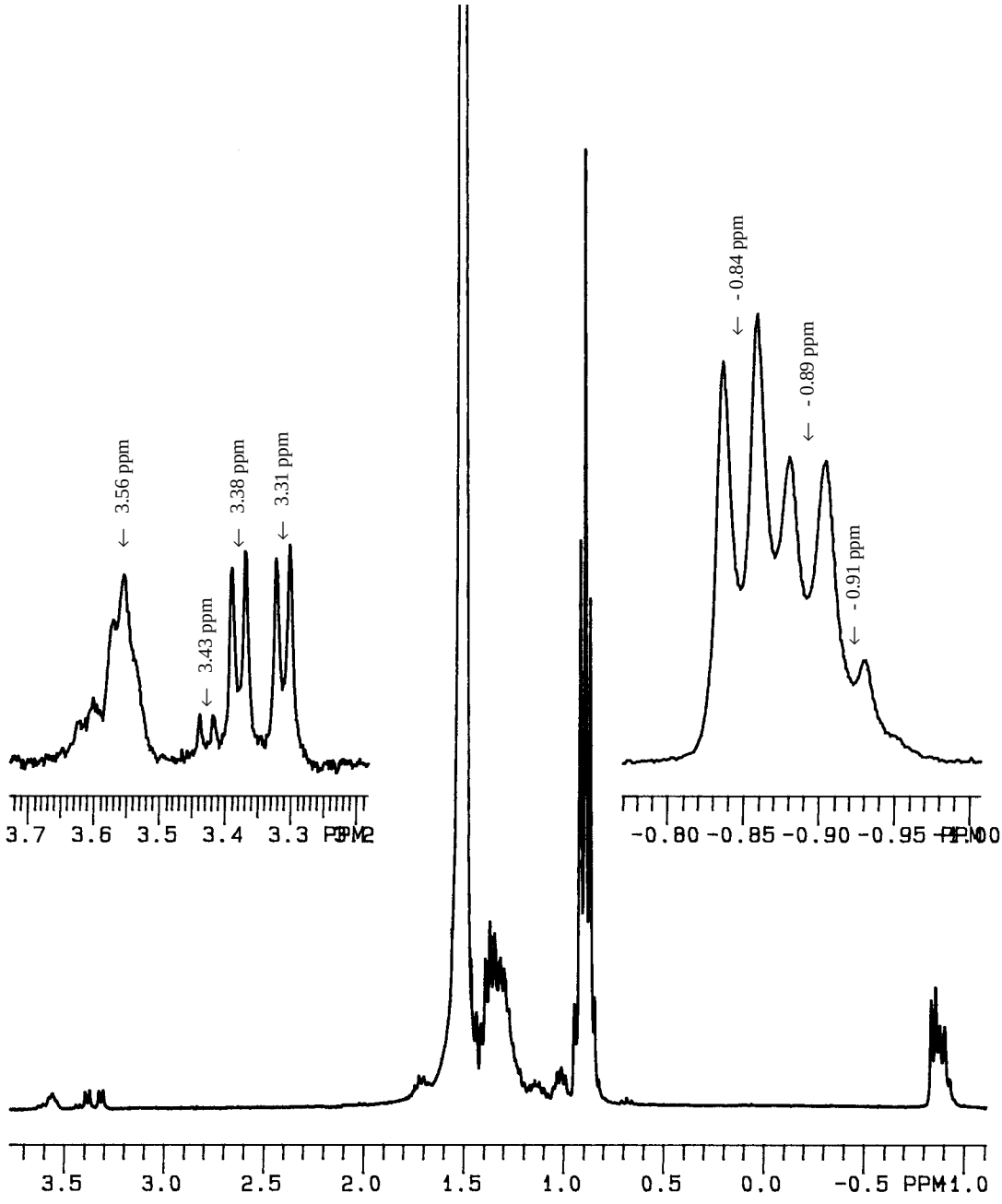


Figure 16 – ^{1}H NMR spectrum of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.4 at – 11.7 °C. Insets show the expansion of the alkoxide alpha proton region (left) and the alkyl alpha proton region (right).

have formed and may have its chemical shift in the same region. The alkoxide alpha proton region also showed some changes. The peaks at 3.56, 3.38 and 3.31 ppm were observed in the previous sample, and the new doublet peak is the 3.43 ppm that has shifted a little upfield from 3.45 at room temperature. This new peak is probably a new mixed aggregate formed in this solution or maybe an aggregate that was already present in the previous sample but now had its amount increased to detectable levels because of the greater O:Li ratio. The correlation of this new peak with the ^{6}Li NMR spectrum can be made by deduction, matching it with a new peak observed in that spectrum.

The ^{6}Li NMR spectra in Figure 17 show a comparison between the two samples (O:Li = 0.2 and 0.4) at room temperature. The two spectra show the same groups of peaks, but with different intensities. The upfield peaks have a greater relative intensity in the sample with higher O:Li ratio, showing that these peaks have grown with more alkoxide groups in solution, as was expected. Decreasing the temperature also shows the same type of changes for this sample (O:Li = 0.4) as was observed with the previous sample. Figure 18 shows the ^{6}Li NMR spectra for this sample at different low temperatures, + 1.3 °C and – 9.3 °C. The downfield peaks that were very broad at room temperature due to interaggregate exchanges become sharper as the temperature decreases and the exchange processes are slowed down (0.88 and 0.47 ppm at – 9.3 °C). The upfield peaks have grown in intensity (– 0.13 and – 0.31 ppm at – 9.3 °C), and a new peak is more pronounced at – 0.49 ppm. This new peak represents a new mixed aggregate that is present in a larger amount in this solution because of the greater concentration of alkoxide groups.

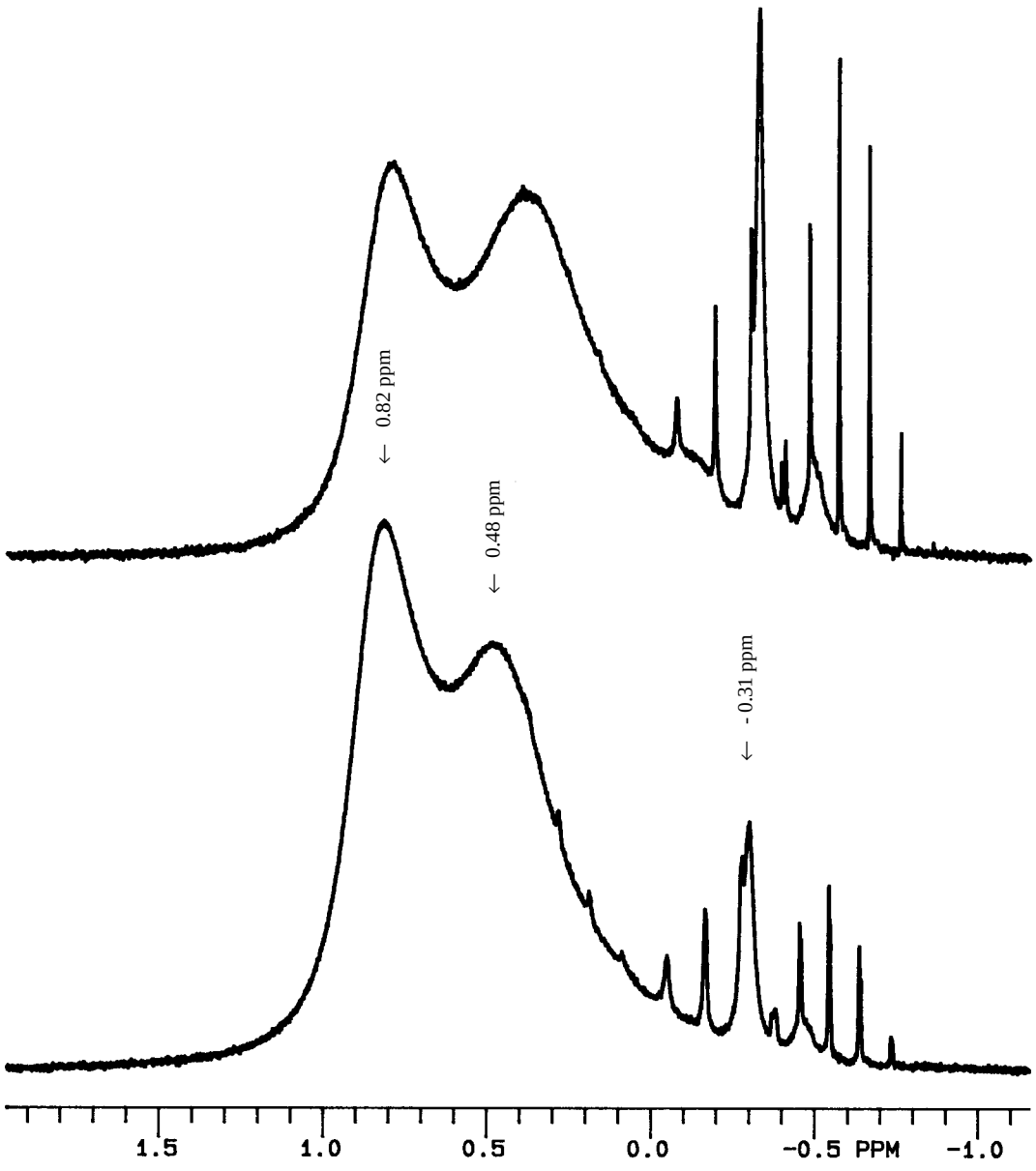


Figure 17 – ^{6}Li {^{1}H} NMR spectra of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.2 (bottom) and with O/Li = 0.4 (top) at room temperature.

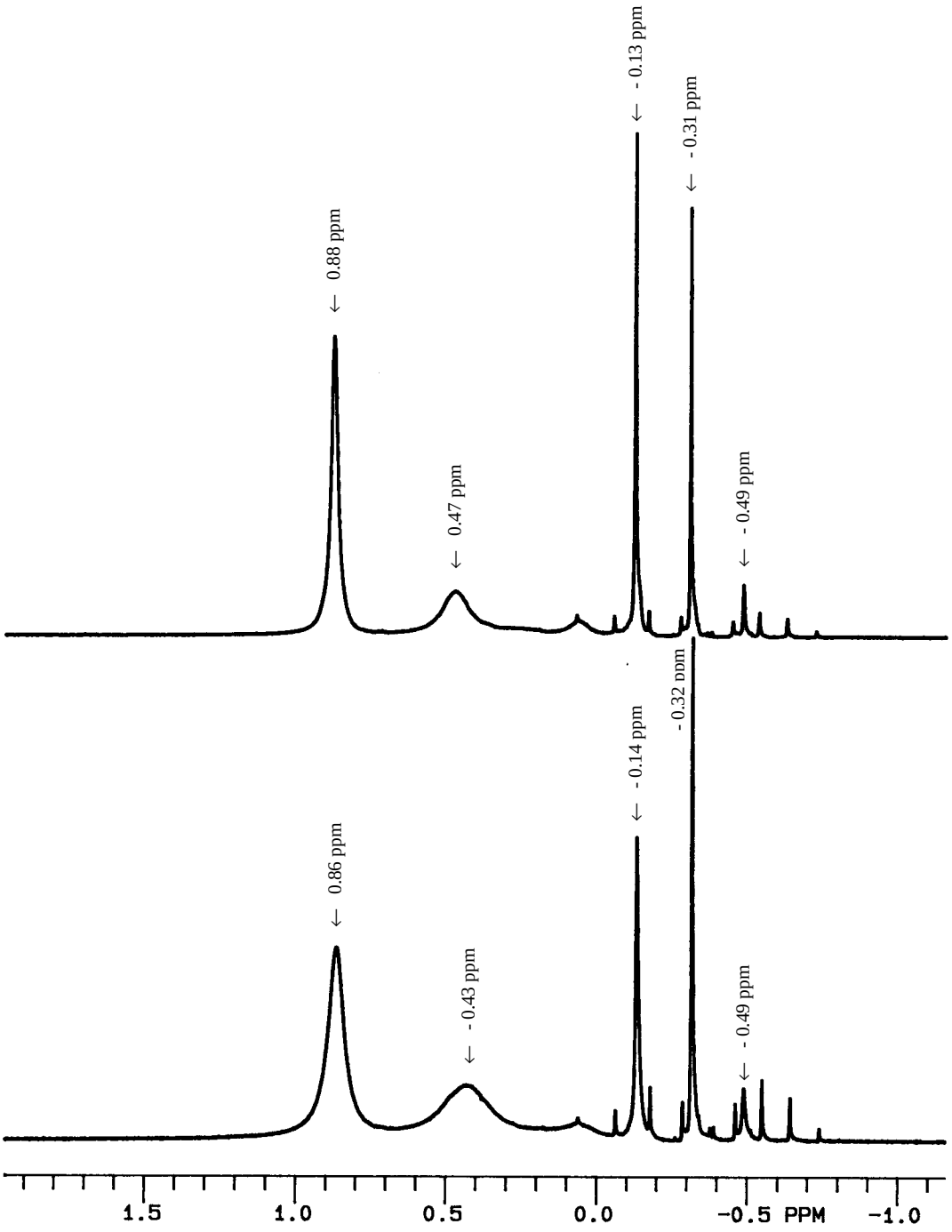


Figure 18 – ^{6}Li {^{1}H} NMR spectra of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.4 at + 1.3 °C (bottom) and at – 9.3 °C (top).

To compare the relative amounts of the different aggregates in solution, Table 5 presents the normalized integration values of the ^{6}Li peaks in these two samples analyzed so far. These normalized integration values were obtained running the spectra with the decoupler turned off to avoid discrepancies due to unequal NOE for different peaks. The integration was not performed at room temperature because of the overlapping peaks could not be integrated properly.

Table 5 – Normalized integration values of the ^{6}Li peaks of 0.2 and 0.4 O:Li ratio samples at low temperatures and the relative amounts of the aggregates in solution.

Sample with O/Li = 0.2		**Sample with O/Li = 0.4**	
At + 5.1 °C (Figure 11)		At + 1.3 °C (Figure 18, bottom)	
Chemical shift /ppm	Relative amount /%	Chemical shift /ppm	Relative amount /%
0.88	52.63	0.86	42.44
0.47	27.07	0.43	29.40
- 0.12	12.18	- 0.14	14.11
- 0.30	8.12	- 0.32	11.57
		- 0.49	2.48
At – 12.3 °C (Figure 12)		At – 9.3 °C (Figure 18, top)	
Chemical shift /ppm	Relative amount /%	Chemical shift /ppm	Relative amount /%
0.87	52.61	0.88	42.83
0.48	18.86	0.47	21.28
- 0.13	19.35	- 0.13	19.71
- 0.32	9.18	- 0.31	13.76
		- 0.49	2.42

These data show the changes of the relative amounts of the aggregates that occur when the O:Li ratio is increased and also when the temperature is lowered. As was

already mentioned, the 0.4 O:Li ratio sample has one more lithium peak present representing a new aggregate that forms in this sample. The trend observed in both samples is that while the peak at 0.88 ppm, which is the peak relative to the alkyllithium aggregate, remains practically unchanged, the mixed aggregate with the lithium peak at 0.47 ppm is decreasing its relative amount and the peak at – 0.12 ppm is increasing. This suggests an equilibrium between the two mixed aggregates, which favor the peak more upfield at lower temperatures. The peak at – 0.32 ppm has also increased at lower temperature, indicating that lower temperature does favor the formation of the aggregates with more alkoxide groups and less alkyl groups.

The integration data of both ^{1}H and ^{6}Li NMR spectra are analyzed together to derive an estimate to what is the ratio of alkyl to alkoxide groups within an aggregate. Given that the number of aggregates is equal to the number of different lithium peaks and that the correlation of those peaks with the alkoxide alpha proton peaks, which can be integrated individually, is known, the integration of the alkyl alpha proton can be calculated. Suppose that all alkyl alpha protons are integrated together while the alkoxide alpha proton peaks are integrated independently of each other, and that sums up to 100%. Then, the integration of the lithium peaks is done, and each peak has a value that also sums up to 100%. So, these represent all the lithium atoms and all the organic chains, represented by the alkyl and alkoxide alpha protons. Because all the alkyl groups were integrated together, the individual value needs to be calculated according to the different aggregates. For example, if one mixed aggregate represents 30 % of the total lithium nuclei and its related alkoxide represents only 10 % of the total organic groups, then the

alkyl groups present in this mixed aggregate must be about 20 % of the total organic groups. That is the unknown value that needed to be calculated, for it was integrated with all alkyl groups. Then, the ratio of alkyl to alkoxide can be calculated as 20 % / 10 %, or 2:1 (two alkyl groups per each alkoxide group in that given aggregate).

This method was applied to the 0.4 O:Li ratio sample using integration data from the ^{1}H NMR spectrum at – 1.2 °C and the ^{6}Li NMR spectrum at 1.3 °C. The alkyl/alkoxide ratios that will result from this approach need to be considered only as estimates due to factors such as: the integration data being used in the calculation are from different NMR spectra and at slightly different temperatures; the integration values may not be accurate; and the fact that other compounds are present in smaller amounts, which also compromises the integration values. This analysis and the results are summarized in Table 6 (on page 69).

The lithium peak at 0.86 did not need to be considered in the alkyl/alkoxide ratio analysis because that is the peak for the alkyllithium hexameric aggregate, which does not have alkoxide groups involved. The alkyl/alkoxide ratios of the peaks at 0.47 and – 0.12 ppm turn out to be the same, 2:1, in spite their different chemical shifts. This is explained by the fact that the lithium chemical shift can vary due to the amount of alkoxide present and also due to the size of the aggregate. For example, two different aggregates, a hexamer and a nonamer, having the same alkyl/alkoxide ratio of 2:1, can be represented by $R_4(RO)_2Li_6$ and $R_6(RO)_3Li_9$, respectively. The lithium chemical shifts of these two aggregates are likely to be different, influenced by the size of the aggregate rather than only the alkyl/alkoxide ratio.

Table 6 – Normalized integration values of the ^{1}H alpha peaks and ^{6}Li peaks of 0.4 O:Li ratio sample at low temperatures and analyses of the alkyl/alkoxide ratio in the mixed aggregates in solution.

Sample with O/Li = 0.4					
^{1}H NMR spectrum at – 1.2 °C			^{6}Li NMR spectrum at + 1.3 °C		
Chemical shift /ppm	Relative amount /%		Chemical shift /ppm	Relative amount /%	
3.56	10.39		0.86	42.44	
3.43	1.54		0.43	29.40	
3.39	4.93		- 0.14	14.11	
3.32	4.70		- 0.32	11.57	
Around - 0.85	78.41		- 0.49	2.48	
Formula **%** of lithium peak **– %** of alkoxide groups **= %** of alkyl groups					
Aggreg.	% of lithium	% of alkoxide	% of alkyl	Alkyl/alkoxide Ratio	Type
1	42.44 % at 0.86 ppm	----------	42.44 % at - 0.84 ppm	----------	alkyllithium
2	29.40 % at 0.44 ppm	10.39 % at 3.56 ppm	19.01 % at - 0.84 ppm	19.01/10.39 **~ 2 : 1**	Mixed agg.
3	14.11 % at - 0.14 ppm	4.70 % at 3.32 ppm	9.41 % at - 0.89 ppm	9.41/4.70 **~ 2 : 1**	Mixed agg.
4	11.57 % at - 0.32 ppm	4.93 % at 3.39 ppm	6.64 % at - 0.91 ppm	6.64/4.93 **~ 4 : 3**	Mixed agg.
5	2.48 % at - 0.49 ppm	1.54 % at 3.43 ppm	14.11 % at not known	0.94/1.54 **~ 3 : 5**	Mixed agg.

However, the data collected so far are not enough to make a definitive assignment of the aggregation states. In this case, the alkyl/alkoxide ratios do not have much value

because the total number of organic groups is not known. The way to investigate the aggregation state of the aggregates in solution is looking at the ^{13}C-^{6}Li coupling pattern observed in the ^{13}C NMR spectrum. This method is very useful to analyze alkyllithium samples at room temperature, as was discussed earlier, but the deviation that occurs with the addition of an atom of oxygen must be considered.

The 0.4 O:Li ratio sample was chosen to do the analyses of alkyl/alkoxide ratios because its results were very similar to the previous sample. The ^{1}H and ^{6}Li NMR spectra have been discussed and lots of similarities between the 0.2 and 0.4 samples were found. Figure 19 shows the expansion of the alkyl alpha carbon region of both samples at different temperatures. These spectra have practically all the same features and the same chemical shifts. As the temperature drops from room temperature to around – 9.0 °C, the broad peak at 19.38 ppm with a shoulder upfield starts to resolve into different broad peaks. At – 9.0 °C, the peaks are 19.49, 19.15, 18.67, 17.75 ppm, in addition to an alkane sharp peak at 18.44 ppm, and the peak at 19.15 ppm that correspond to the alkyllithium aggregate starts to show multiplet resolution. These data confirm that the two samples are forming the same aggregates, and the only difference is the distribution amounts of these aggregates.

Unfortunately, the only peak that shows some multiplet resolution is the one at 19.15 ppm, which has already been characterized as the hexameric alkyllithium aggregate. The other peaks in the alpha carbon region do not resolve into multiplets and their coupling can not be determined. To show that these peaks really are coupled to various lithium nuclei in different aggregates, a ^{13}C $\{^{1}H,^{6}Li\}$ NMR spectrum was

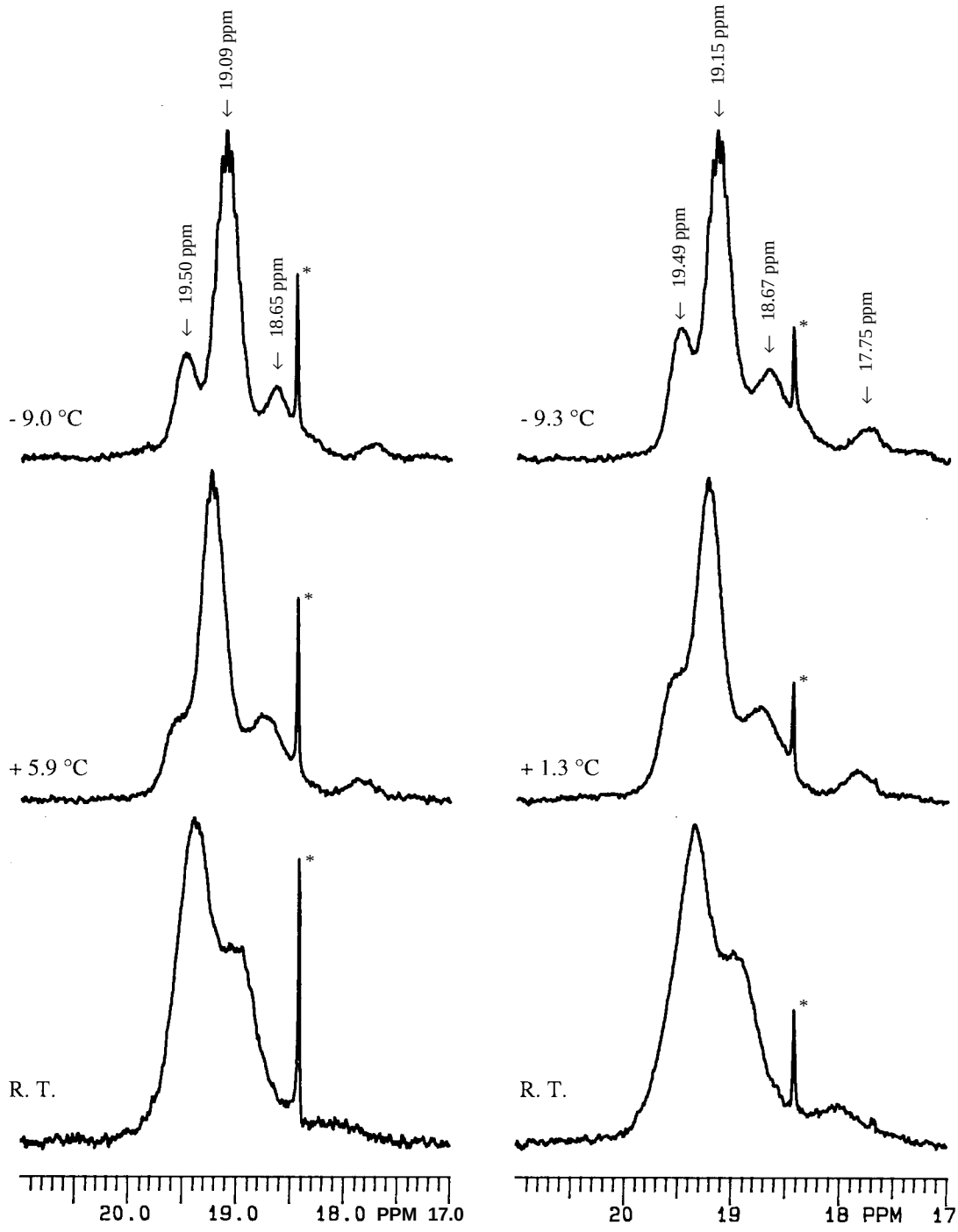


Figure 19 – ^{13}C NMR spectra of the alpha carbon region of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.2 (left) and with O:Li = 0.4 (right) at different temperatures. Asterisks indicate an alkane peak (18.44 ppm).

obtained. This is a normal 1D NMR spectrum with only one difference, which is the ability to simultaneously decouple ^{1}H and ^{6}Li nuclei. An expansion of the alpha carbon region of this spectrum is shown in Figure 20, in comparison with a spectrum where only ^{1}H nuclei were decoupled. This spectrum shows that the broad peak at 19.49 ppm was actually the overlap of two peaks at 19.52 and 19.42 ppm that were observed to collapse to sharp singlets due to ^{6}Li decoupling. The alkyllithium peak at 19.15 ppm also collapses into a singlet at 19.13 ppm.

The other two broad peaks at 18.67 and 17.75 ppm observed previously did not become sharper with the ^{6}Li decoupling and they were almost buried in the base line. This fact may be related to the fact that even in the ^{6}Li NMR spectrum there are broad peaks that seem to be exchanging and that would affect the coupling, because the spread of the magnetization of this peak is very large. An experiment that could also determine the correlation of these alpha carbon peaks to the lithium peaks is the ^{13}C-^{6}Li 2D NMR HETCOR. An attempt to obtain this spectrum was made, but it was not successful. No signal was obtained and, consequently, no correlation could be seen. Another 2D NMR spectrum could be attempted to show the correlation between carbon and protons, the ^{13}C-^{1}H 2D NMR HETCOR. This experiment was not done due to the constraint of time for this research.

The triple resonance probe, custom made for this research group which allowed the ^{6}Li nuclei to be decoupled in the ^{13}C NMR spectrum, is also used for other special experiments. One of these special experiments performed on the 0.4 O:Li ratio sample was the ^{6}Li *J*-modulated ^{13}C spin-echo NMR spectrum.[11] This experiment refocuses the

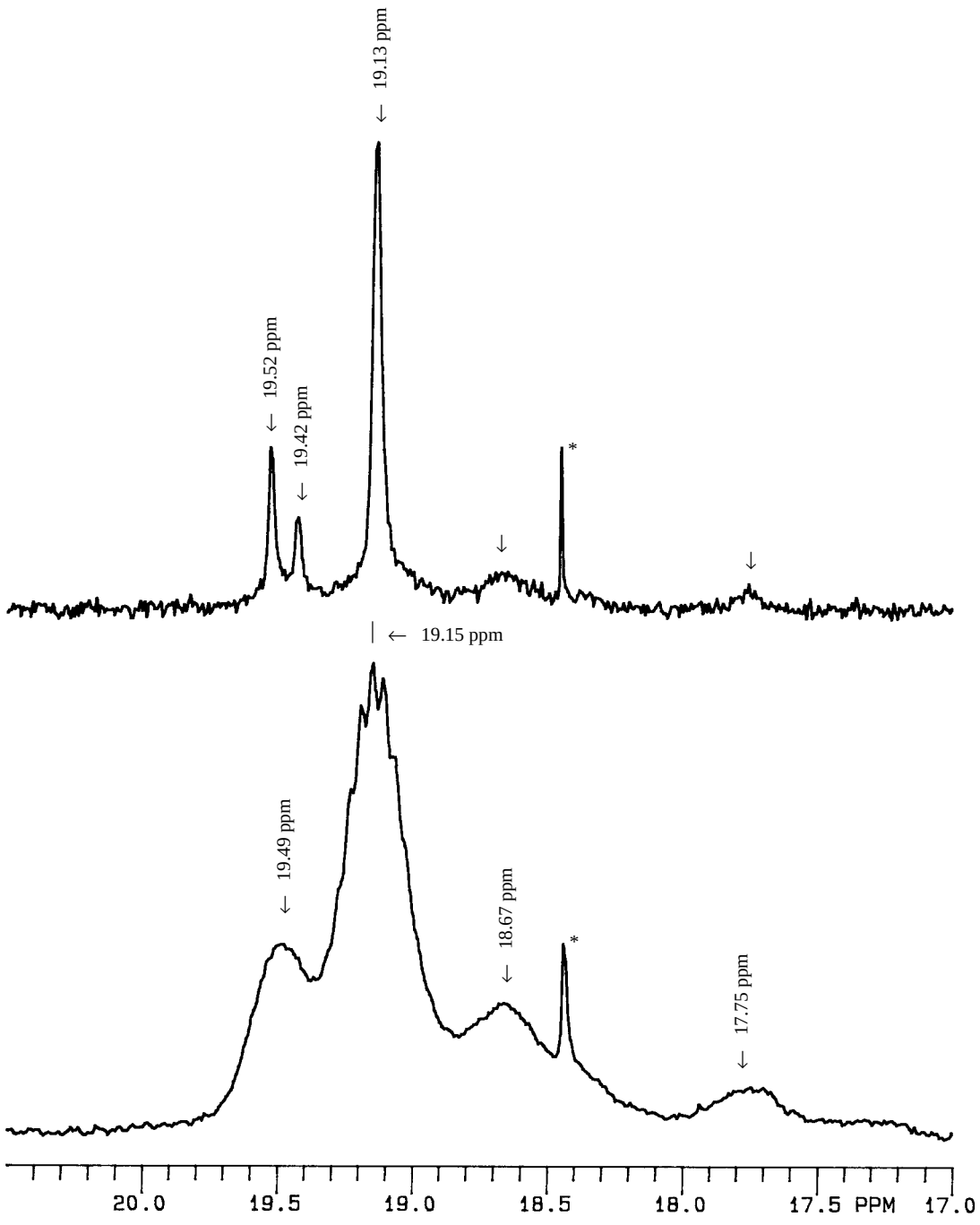


Figure 20 – ^{13}C NMR spectra of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.4 at – 9.3 °C (bottom) and ^{13}C {^{1}H, ^{6}Li} NMR spectrum at – 11.7 °C (top). Asterisks indicate and alkane peak (18.44 ppm).

^{13}C magnetization, setting a delay in the pulse sequence according to the magnitude of the ^{13}C-^{6}Li coupling constant. The delay must equal $1/J_{obs}$ (D2 = $1/J_{obs}$; J_{obs} = ^{13}C-^{6}Li observed coupling) to be able to refocus the carbon peak with that specific coupling. The carbon peak will also be refocused in multiples of the delay time, but the intensity of the peak will decrease.

The constant coupling observed for the alkyllithium alpha carbon peak is 3.19 Hz. This coupling gives a delay of 0.314 s to refocus that peak. If other peaks have the same coupling constant, even if was not possible to observed, these peaks also will refocus at the delay time of 0.314 s. This would give experimental evidence that other peaks have the same coupling, and they could probably be assigned as hexamers because the alkyllithium is known to be a hexamer. This assignment is by association, for the magnitude of the coupling is related to how many lithium nuclei is coupled to the carbon. However, this analogy is valid for different aggregates of alkyllithium compounds, and, when an alkoxide is introduced in the aggregate, the magnitude of the coupling may be altered.

Figure 21 shows a series of ^{6}Li *J*-modulated ^{13}C spin-echo NMR spectra in comparison with the ^{13}C {^{1}H, ^{6}Li} NMR spectrum. The first spectrum of the series has a delay of 0.314 s so that the alkyllithium would be refocused and any other peak with the same coupling would refocus too. The other three spectra have delays of 0.418 s, 0.470 s and 0.625 s that were calculated to refocus a carbon that would be coupled to 8, 9 and 12 lithium nuclei. These calculations considered an average coupling from the observed coupling of the hexamer. If the delays really represented the estimated number of lithium

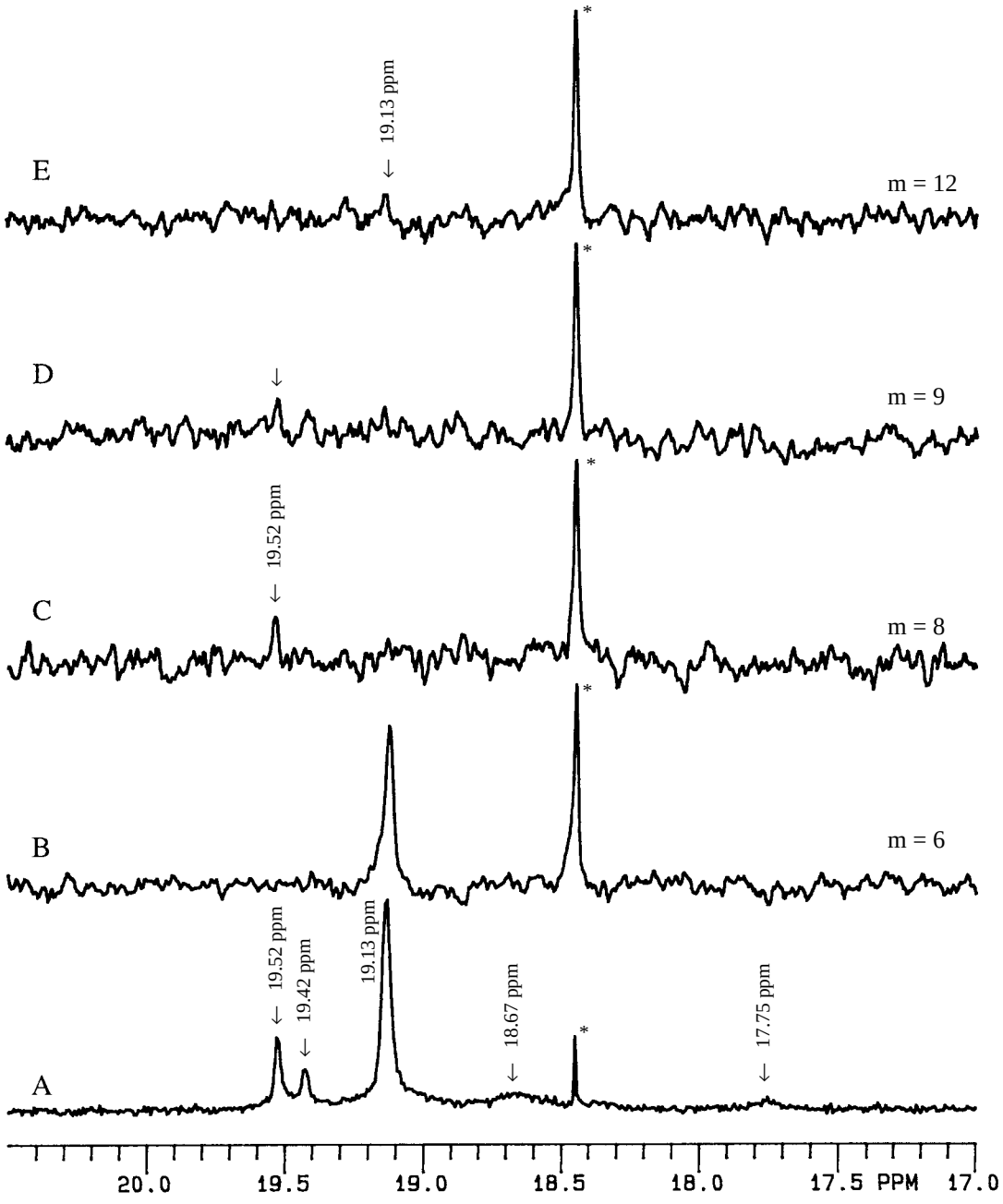


Figure 21 – ^{13}C {^{1}H, ^{6}Li} NMR spectrum of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.4 (A), and ^{6}Li *J*-modulated ^{13}C NMR spectra with different delays; D2 = 0.314 s (B) for m = 6, D2 = 0.418 s (C) for m = 8, D2 = 0.470 s (D) for m = 9 and D2 = 0.625 s (E) for m = 12. Asterisks indicate an alkane peak (18.44 ppm).

nuclei coupled to the carbons and peaks were observed, those peaks could be assigned as octamers, nonamers and dodecamers.

As was expected, the alkyllithium alpha carbon peak at 19.13 ppm did refocus in the spectrum set for a carbons coupled to six lithium (m = 6), but no other peak was observed. In the second spectrum of the series (m = 8), the peak at 19.52 ppm appears to be refocusing and it also seems to have some magnetization on the third spectrum (m = 9). No other peaks were observed, except for some magnetization showing the alkyllithium refocusing in the fourth spectrum (m = 12) with very low intensity. This was possible because the peaks can also refocus at multiples of the delay set for their peaks, as was mentioned above.

These results seem to indicate that at least one of the mixed aggregates is possibly an octamer or a nonamer. Because no correlation was obtained between the carbon spectrum and the lithium or proton spectrum, this aggregate can not be identified properly. An important result of this experiment is the evidence for the formation of a larger aggregate than the original alkyllithium hexamer.

Mixture of alkyllithium with lithium alkoxide (O:Li = 0.2)

It has been shown that alkyllithium/lithium alkoxide mixed aggregates are formed when 2-ethyl-1-butyllithium reacts with 2-ethyl-1-butanol in cyclopentane solution. Mixed aggregates are known to exist even if the starting reagents have different alkyl groups.[6] The mechanisms by which these mixed aggregates are formed in solution is not well known, but the reaction may be involved. Therefore, it was not obvious if the simple

mixture of an alkyllithium with the corresponding lithium alkoxide would form the same mixed aggregates. Because no reaction is involved when an alkyllithium compound is mixed with a lithium alkoxide, the formation of mixed aggregates would be related to exchange processes between aggregates.

As it was described in Chapter II, the lithium 2-ethyl-1-butoxide prepared independently from the alkyllithium was not very soluble in cyclopentane. The sample prepared was intended to have approximately the O:Li ratio of 0.2, as the previous sample analyzed, but the lithium alkoxide did not dissolve completely in cyclopentane. Therefore, the amounts of the mixed aggregates, if they do form, are expected to be different.

The ^{1}H, ^{13}C and ^{6}Li NMR spectra for this sample were analyzed both at room temperature and at lower temperature. Figure 22 shows the expansion of both the alkyl and alkoxide alpha proton regions at two different temperatures. There is one doublet peak at – 0.83 ppm in the alkyl alpha proton region at room temperature that must correspond to the alkyllithium aggregate. This doublet is not as sharp and well resolved as the doublet observed in the alkyllithium sample, which probably indicates the presence of another doublet overlapping. Also, this spectrum shows a doublet at 3.57 ppm in the alkoxide alpha proton region that indicates the presence of an alkoxide group in solution that is possibly related to a mixed aggregate. In fact, a doublet with the same chemical shift was observed in the sample with 0.2 O:Li ratio. These data point to the formation of at least one mixed aggregate. The low temperature spectrum shows that the alkyl alpha proton doublet resolves into two doublets at – 0.84 and – 0.89 ppm. In the alkoxide alpha

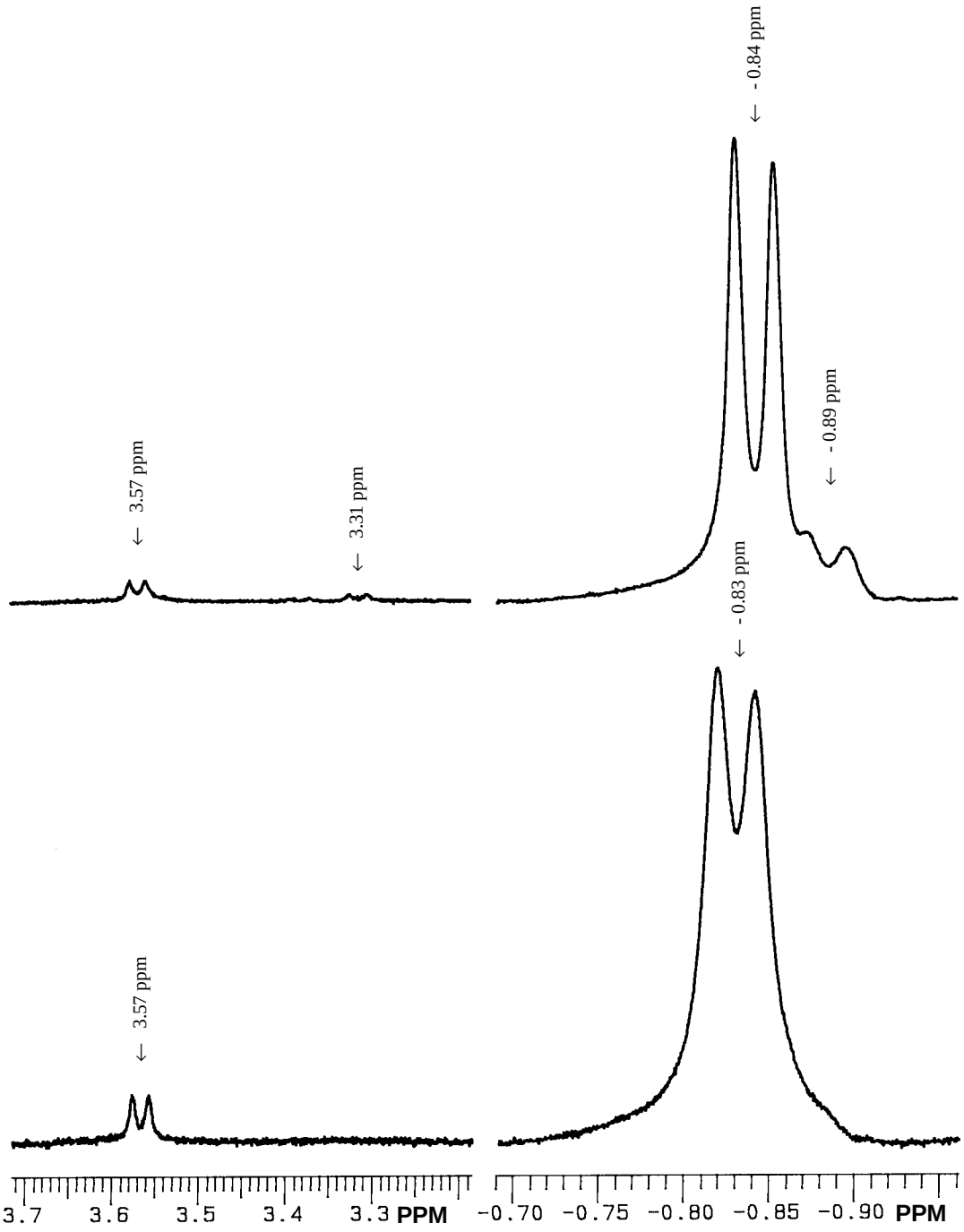


Figure 22 – ^{1}H NMR spectra of mixed 2-ethyl-1-butyllithium and lithium 2-ethyl-1-butoxide with O:Li = 0.2, at room temperature (bottom) and at – 10.5 °C (top). Expansions of the alkoxide alpha protons (left) and the alkyl alpha protons (right) with same vertical scale.

proton region the doublet at 3.57 ppm decreases in intensity and a very small doublet at 3.31 ppm can be observed. These data are in accordance with was observed in the previous sample and show the formation of aggregates at low temperature.

Figure 23 shows the ^{6}Li NMR spectra at room temperature and – 10.5 °C. These spectra also show similarities with the spectra from previous samples. At room temperature, there are two broad peaks at 0.87 and 0.52 ppm. When the temperature is lowered, the broad peaks become sharper at 0.88 and 0.50 ppm and a small peak at – 0.12 ppm is now observed. These are the same peaks observed for the sample with 0.2 and 0.4 O:Li ratio. Therefore, these peaks should correspond to the same aggregates.

The ^{13}C NMR spectra in Figure 24 at room temperature and Figure 25 at – 6.4 °C also show similar peaks. The alpha carbon peak at 19.37 ppm at room temperature from the alkyllithium aggregate shows a shoulder at 18.99 ppm that must correspond to the mixed aggregate. In the alkoxide alpha carbon region, there is only one peak at 66.30 ppm, which makes clear the assignment of this mixed aggregate. At lower temperature, the shoulder in the alkyl alpha carbon peak is shifted more upfield, and the peaks appear at 19.13 and 18.65 ppm. At this temperature, the alkyllithium alpha carbon peak shows some multiplet resolution as was observed in the previous sample, around the same temperature.

These are the same observations made for the previous sample so that it is clear that this alternative procedure of sample preparation leads to the same results. The only drawback in using this sample was the problem caused by the poor solubility of the lithium alkoxide, which not only remained as a precipitate in solution, preventing from a

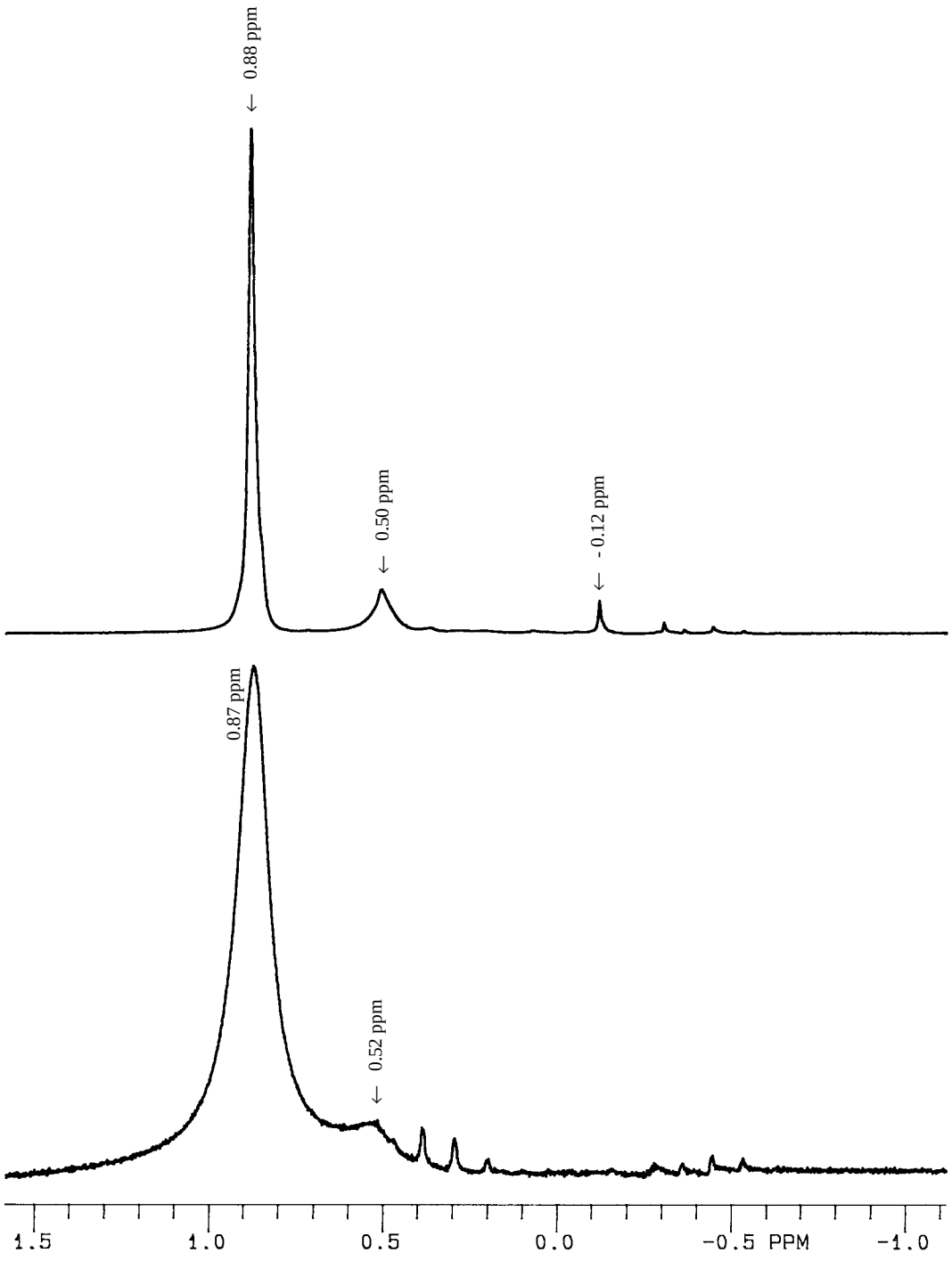


Figure 23 – ^{6}Li NMR spectra of mixed 2-ethyl-1-butyllithium and lithium 2-ethyl-1-butoxide with O:Li = 0.2 at room temperature (bottom) and at – 10.5 °C (top).

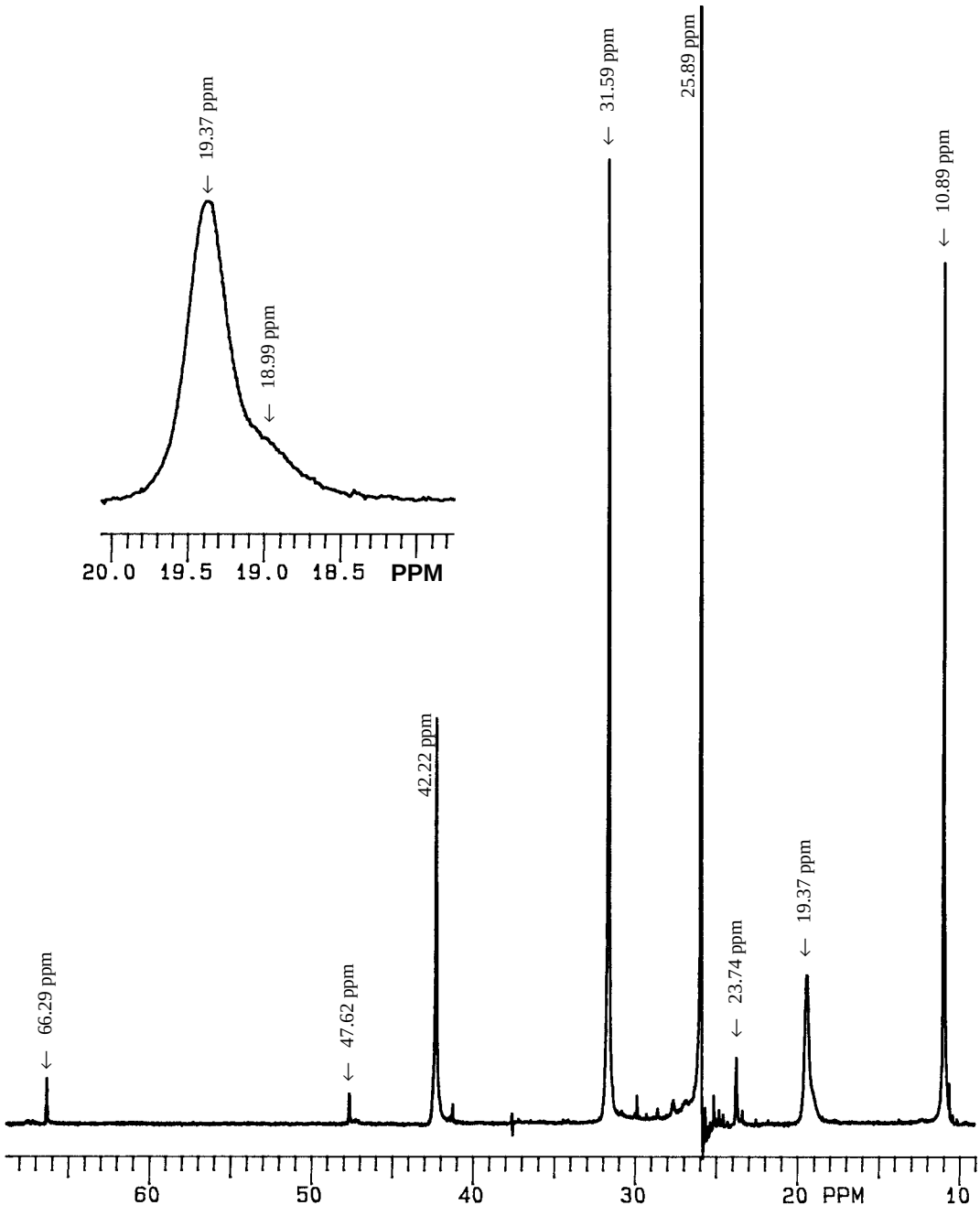


Figure 24 – ^{13}C NMR spectrum of mixed 2-ethyl-1-butyllithium and lithium 2-ethyl-1-butoxide with O:Li = 0.2 at room temperature. Inset shows an expansion of the alpha carbon region.

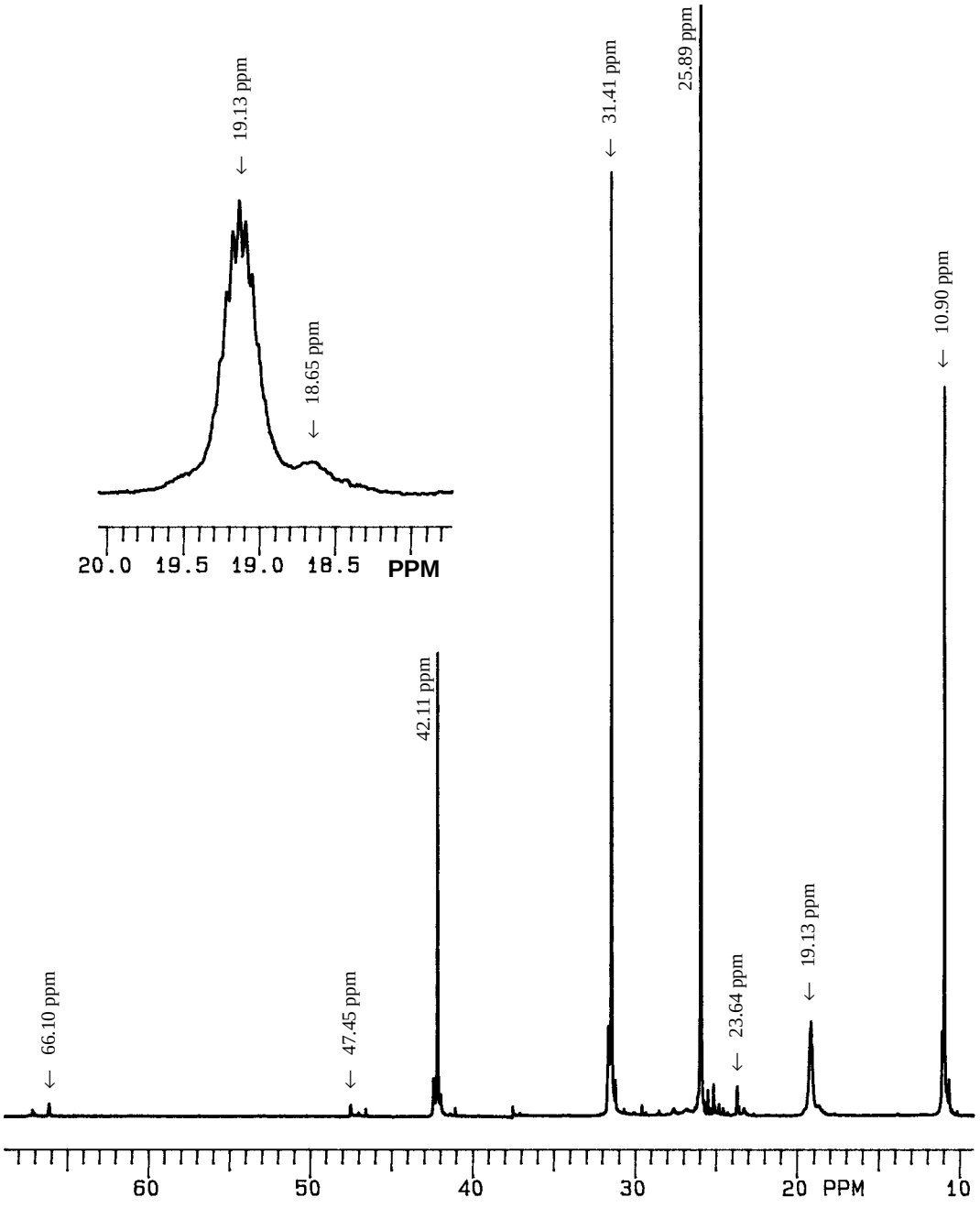


Figure 25 – ^{13}C NMR spectrum of mixed 2-ethyl-1-butyllithium and lithium 2-ethyl-1-butoxide with O:Li = 0.2 at – 6.4 °C. Inset shows an expansion of the alpha carbon region.

good shimming of the sample, but also hindered the formation of larger amounts of the alkyllithium/lithium alkoxides mixed aggregates.

The small amount of mixed aggregates that formed in this sample and the observation that the lithium alkoxide stayed mostly as a precipitate in solution indicate that the solid form of the lithium alkoxide is more stable in cyclopentane. If the lithium alkoxide's solubility could be improved by heating up the solution, maybe the amount of mixed aggregates would be greater. However, that idea was not carried out because of the risk of decomposing the alkyllithium compound and its aggregates. What was really interesting about this sample was finding out that simply mixing alkyllithium and lithium alkoxide led to the formation of the same type of mixed aggregates that were formed when alkyllithium reacts with alcohol.

O:Li = 0.6

Increasing the O:Li ratioresults in the formation of new species in solution. This is observed in all NMR spectra acquired at room temperature. Figure 26 shows the ^{1}H NMR spectrum of this sample at room temperature. The presence of new species is observed by the appearance of new peaks in the alkyl alpha protons region at around – 0.90 ppm and also in the alkoxide alpha proton region at around 3.50 ppm. The integration of all the peaks in these two regions indicates that the alkoxide alpha protons correspond to 64.3 % and the alkyl alpha protons correspond to 35.7 %. This distribution corresponds to a O:Li ratio of 0.64 that is close to the ratio intended of 0.6. The difference from this spectrum to the spectra of the samples with low O:Li ratios is the appearance of many peaks with

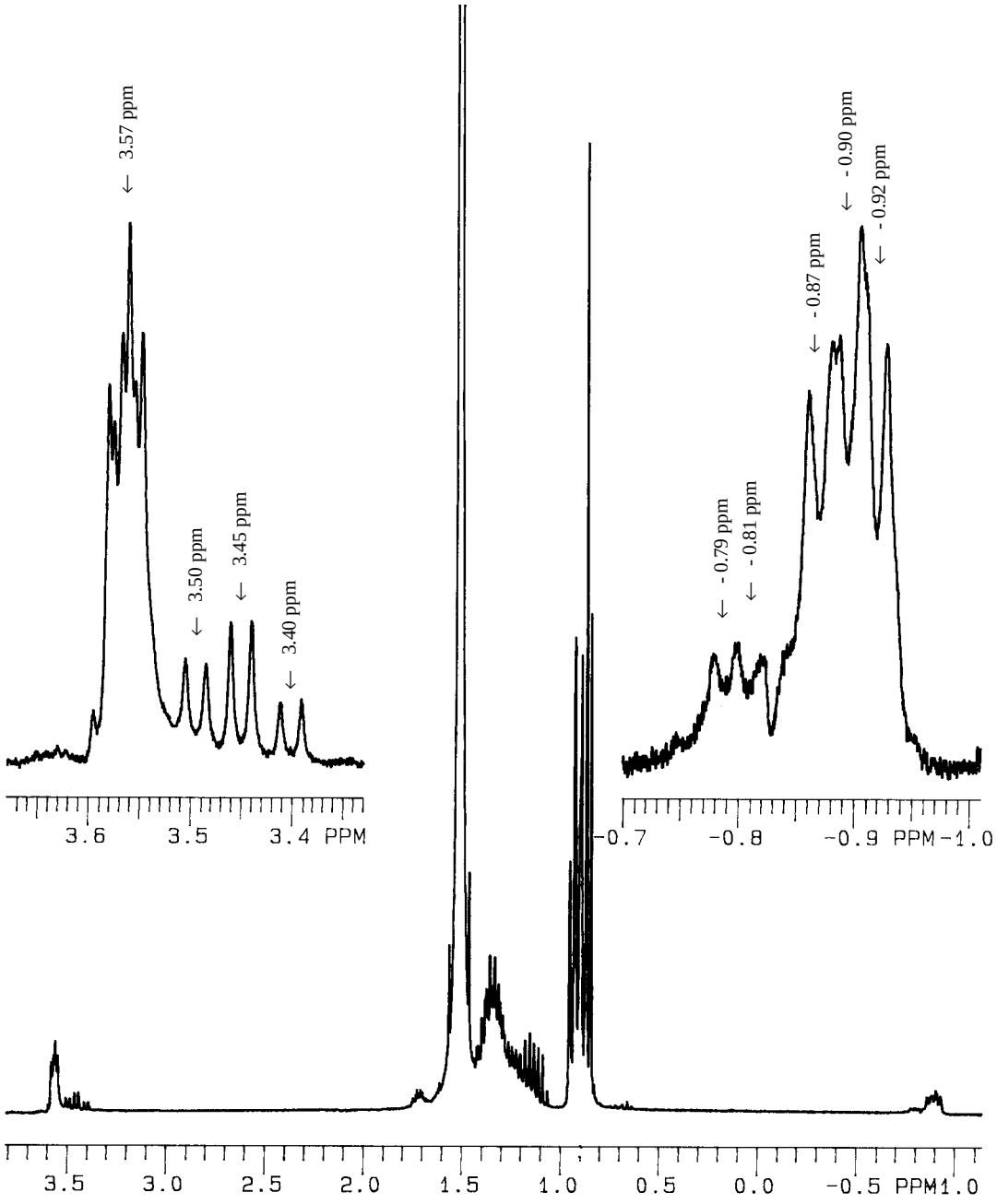


Figure 26 – ^{1}H NMR spectrum of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.6 at room temperature. Insets show the expansion of the alkoxide alpha proton region (left) and the alkyl alpha proton region (right).

different chemical shifts. These peaks are in the same region of the peaks observed earlier for the low O:Li ratios, but it is difficult to determine if they are the same because the peaks are overlapping. Due to the higher O:Li ratio, these peaks are more likely to be peaks from new species formed in solution, possibly new mixed aggregates with a larger number of alkoxide groups per aggregate.

Broad peaks due to the overlap of different doublets are observed in both alkyl and alkoxide alpha proton regions. However, there are three doublets that are not overlapping in the alkoxide alpha proton region, and their chemical shifts are 3.50, 3.45 and 3.40 ppm. The 3.45 and3.40 ppm peaks were present in the previous samples, but the 3.50 ppm peak is new to this sample. This is also indication that new peaks are present and overlapping at around 3.57 ppm. This ^{1}H NMR spectrum suggests that some of the mixed aggregates observed earlier are still present, and new aggregates are formed in this sample with greater O:Li ratio. The analysis of this spectrum alone is not sufficient to determine how many aggregates are in solution and the assignment of the peaks to these aggregates; therefore, more data will be analyzed.

The ^{13}C NMR spectrum of this sample at room temperature, shown in Figure 27, also indicates the presence of multiple aggregates, since there are multiple peaks around the alkyl alpha carbon region from 17 to 20 ppm. There are at least six alkyl alpha carbon peaks present at 19.54, 19.31, 19.05, 18.17, 17.90 and 17.56 ppm. Due to unresolved coupling between the alpha carbon and the ^{6}Li nuclei in the aggregates, these peaks are small and broad, and the overlap between the peaks could be hiding even more peaks, making it difficult to determine how many alpha carbon peaks there are. There is also the

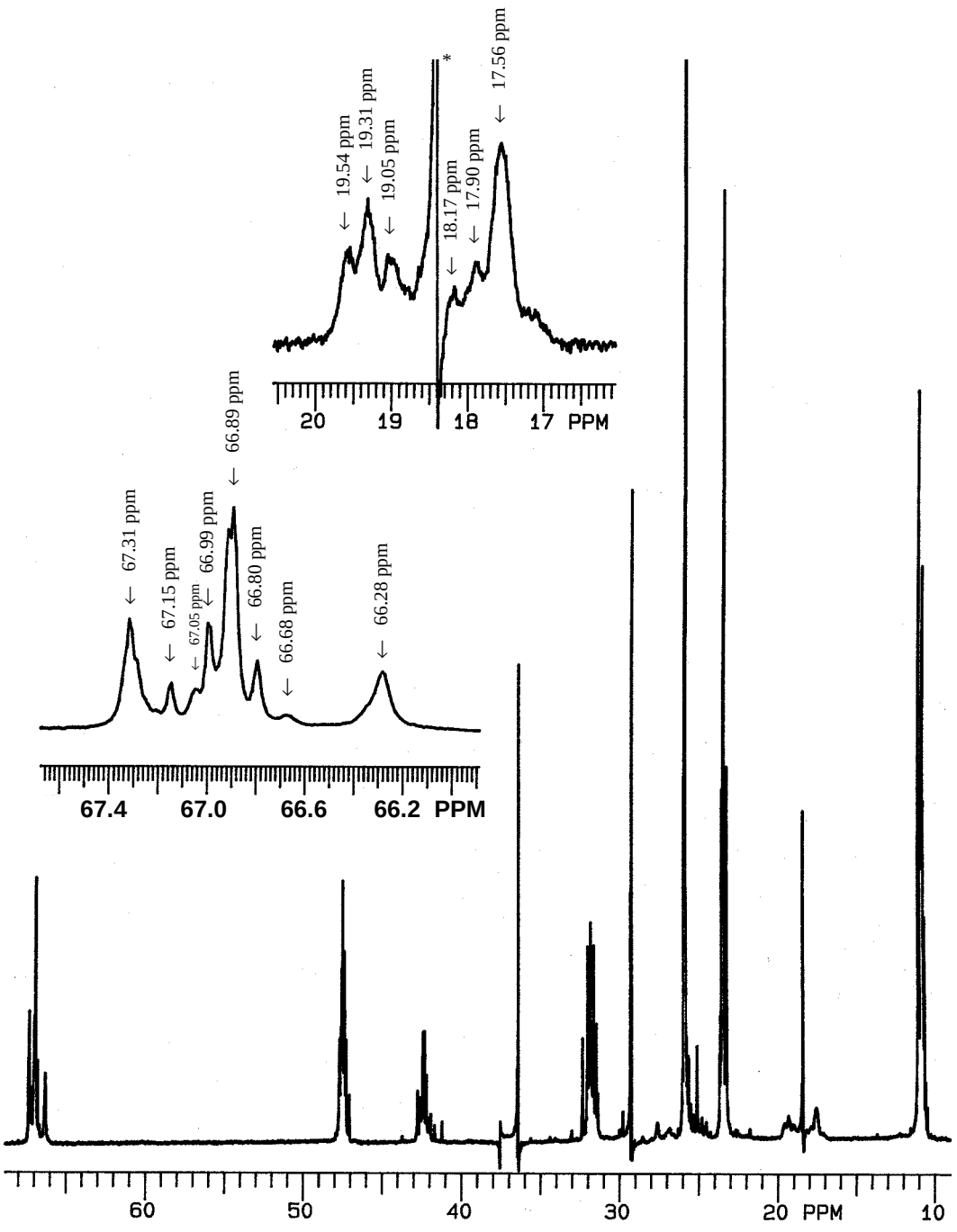


Figure 27 – ^{13}C NMR spectrum of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.6 at room temperature. Insets show the expansion of the alkoxide alpha carbon region (lower left) and the alkyl alpha carbon region (upper left). Asterisk indicates an alkane peak (18.44 ppm).

interference of the sharp peak observed at 18.44 ppm that is from one of the carbons in the alkane formed when the alkyllithium reacts with the alcohol.

Multiple peaks are also observed in the alkoxide alpha carbon region at around 67 ppm. In this region, eight peaks are observed at 67.31, 67.15, 67.05, 66.99, 66.89, 66.80, 66.68 and 66.28 ppm, indicating eight magnetically different alkoxide groups. The peaks at 67.31 and 66.89 ppm are a little broader than the other peaks. This could be due to the overlap of different peaks, indicating that the total number of different alkoxide groups could be higher than eight.

The ^{6}Li NMR spectrum of this sample is shown in Figure 28 at room temperature and – 9.6 °C. These spectra were also run with the ^{1}H decoupler turned off so that peaks coupled to hydrides could be identified. These spectra are not shown because no changes were observed in the major peaks, which indicates that no hydride ions are present or they were in such small amounts that they could not be detected. The broad peaks in the room temperature spectrum become sharper in the low temperature spectrum, indicating that some interaggregate exchange processes have been slowed down. No peaks are observed in the downfield region where a lithium peak for the exclusive alkyllithium aggregate would be. Therefore, all the peaks observed must be related to mixed aggregates and possibly a small amount of exclusive lithium alkoxide aggregates. These mixed aggregates likely have a higher alkoxide/alkyl ratio because the lithium peaks are shifted more upfield than the others observed before. Due to the higher O:Li ratio of this sample, there are more alkoxide groups than alkyl groups in solution, and it is reasonable to assume the aggregates are richer in alkoxide groups. There are peaks with the same

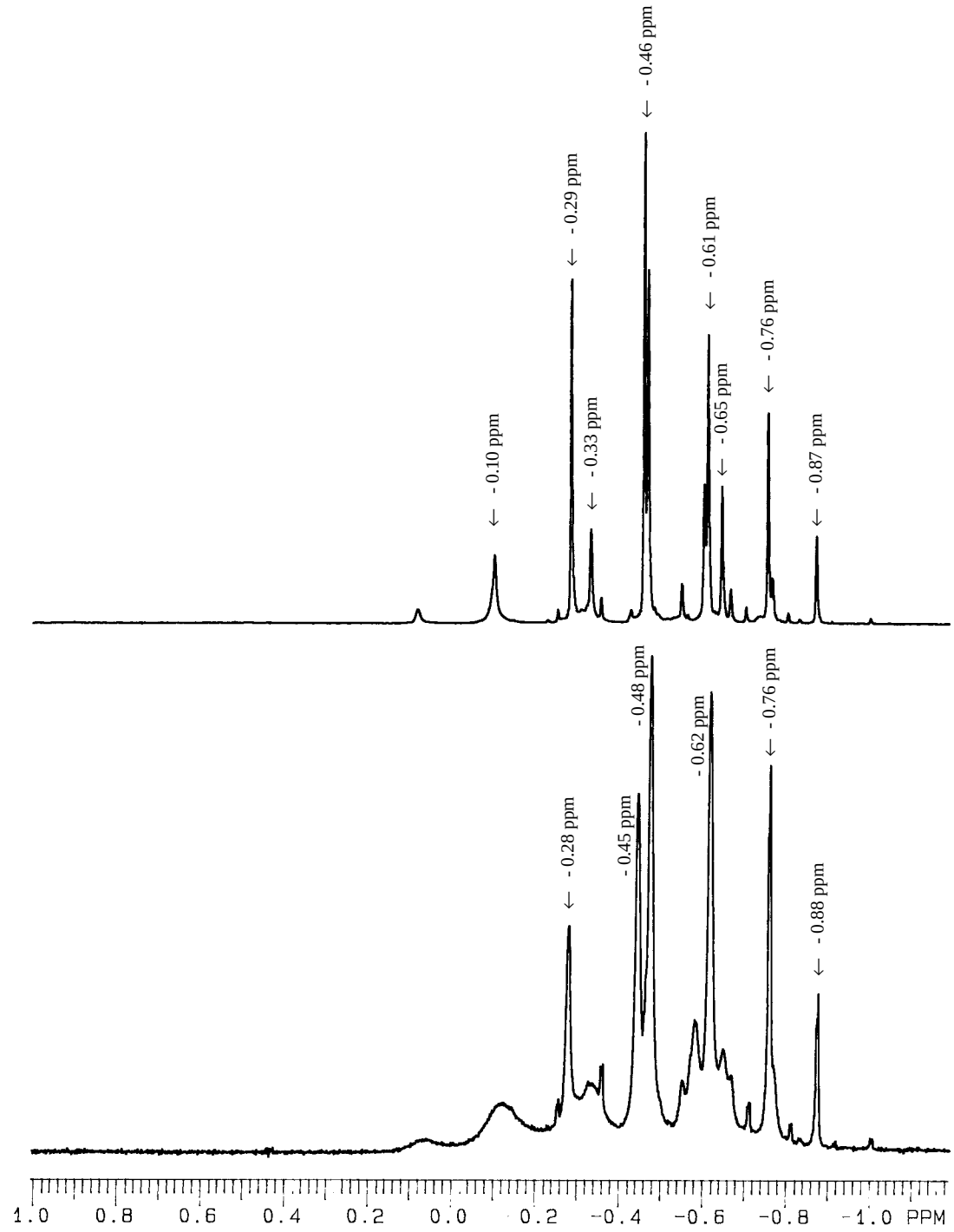


Figure 28 – ^{6}Li NMR spectrum of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 0.6 at room temperature (bottom) and at – 9.6 °C (top).

chemical shift observed before for sample with low O:Li ratio that probably correspond to the same aggregates already studied, but they have small intensities compared to the other peaks, which indicate that they are present in small amounts.

The conclusion is that new aggregates are formed with higher O:Li ratio, and these aggregates are possibly larger in size and richer in alkoxides, but the analyses carried so far were not enough to determine their aggregation states and their composition.

O:Li = 1 from alkyllithium/alcohol mixture and independently prepared lithium butoxide

An attempt to prepare a sample where all the alkyllithium was going to be converted to alkoxide was made, but it was not successful. Differences in the amounts of alcohol and alkyllithium made the ratio less than 1, so that some alkyllithium remained in solution. The presence of the remaining alkyllithium was verified by the NMR spectra obtained for this sample. Both ^{1}H and ^{13}C NMR spectra in Figure 29 and Figure 30, respectively, show the presence of peaks in the regions respective to the alpha carbon. The ^{1}H NMR spectrum shows several small doublet peaks in the region around – 0.8 ppm, where the alkyl alpha protons normally appear. It also shows a great increase in the intensity of the peaks in the alkoxide alpha protons region, as was expected. The integration of the alkyl and alkoxide alpha proton regions showed the O:Li ratio equal to 0.83. The solution to this problem would have been the use of alcohol in excess to ensure the conversion of all alkyl groups into alkoxides. This procedure would leave the excess

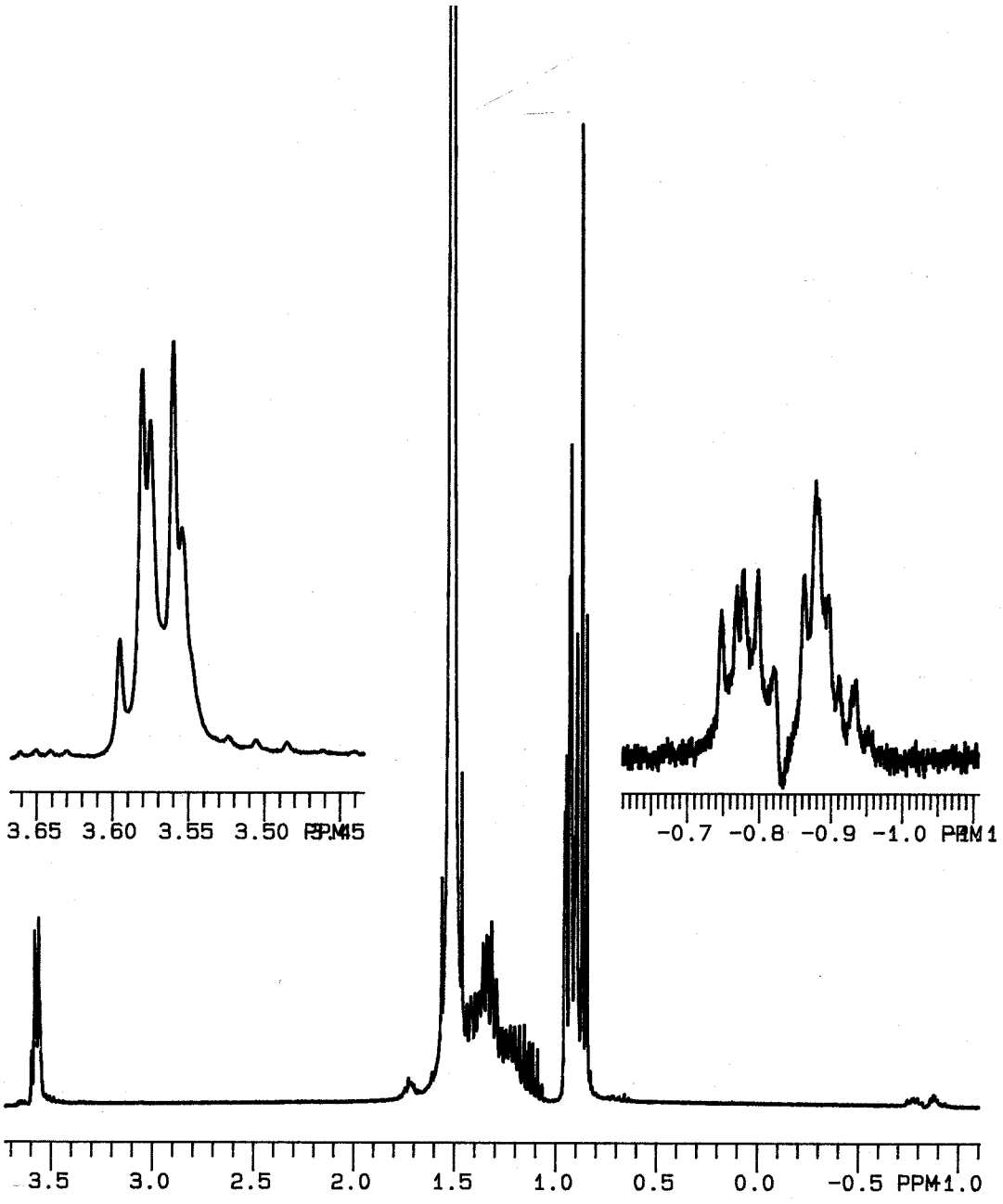


Figure 29 – ^{1}H NMR spectra of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 1. Insets show expansion of the alkoxide alpha proton region (left) and the alkyl alpha proton region (right).

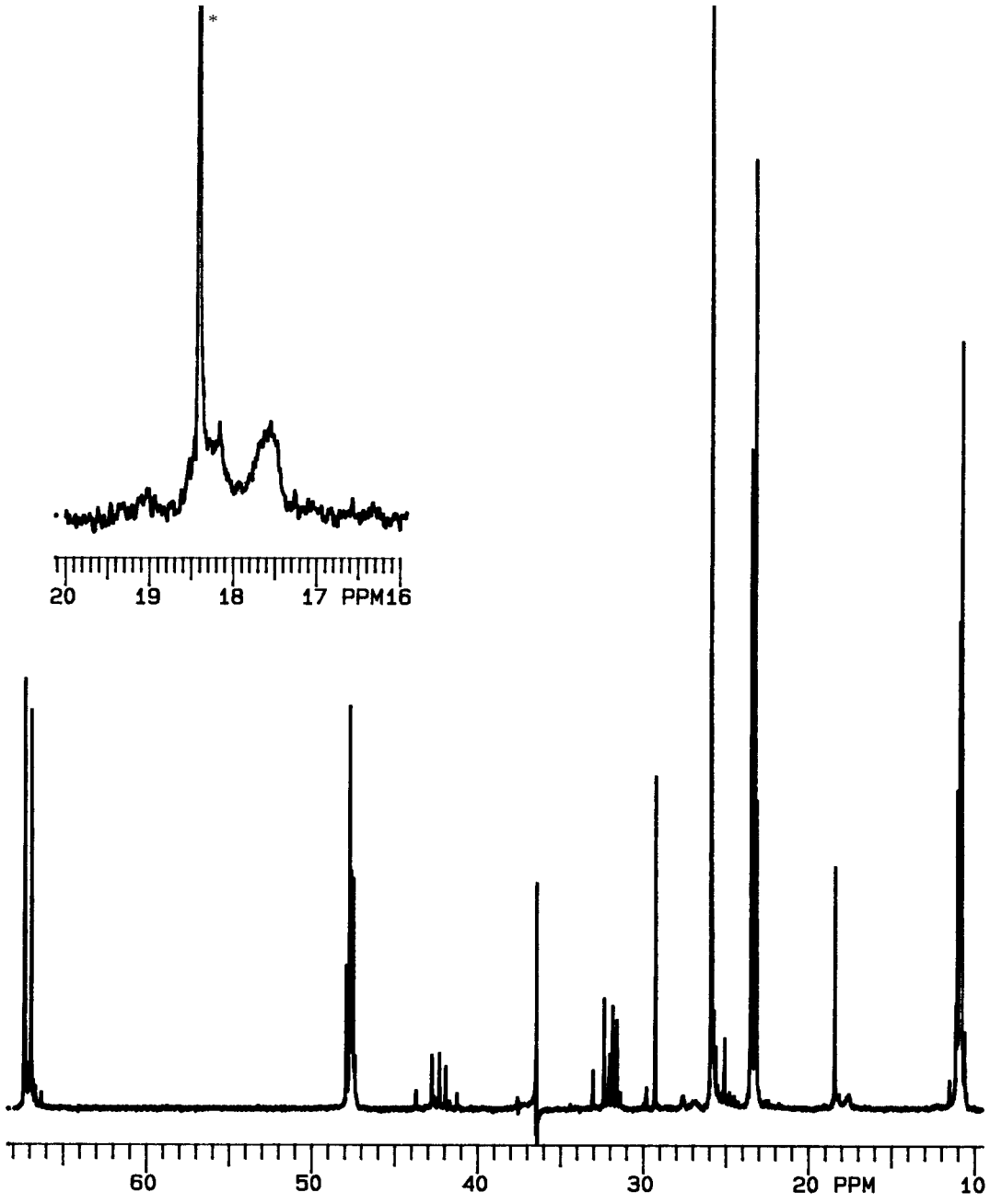


Figure 30 – ^{13}C NMR spectrum of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 1. Inset shows expansion of the alkyl alpha carbon region. Asterisk indicates an alkane peak (18.44 ppm).

alcohol in solution as well as the alkane that forms as a byproduct of the reaction with the alkyllithium.

The ^{13}C NMR spectrum also shows small broad peaks in the alkyl alpha carbon region between 17 and 19 ppm and a great increase of the peaks in the alkoxide alpha carbon region around 67 ppm. This is further evidence of remaining alkyl groups in the sample. This sample was not extensively studied and the determination of the characteristics of the aggregates present were not done at this time.

Figure 31 shows the ^{6}Li NMR spectrum of this sample in comparison to the NMR spectrum of the lithium 2-ethyl-1-butoxide sample that was prepared independently, as discussed in Chapter II. Due to the poor solubility of this lithium alkoxide in cyclopentane solution, the sample tube had a large amount of solid precipitate floating in the solution that resulted in a low resolution spectrum because the sample could not be properly shimmed. However, the comparison can still be made. Six major ^{6}Li peaks are present in the mixed sample at – 0.48, – 0 .62, – 0 .76, – 0.77, – 0.87 and – 1.00 ppm and the lithium alkoxide sample shows three peaks at – 0.93, – 0.96 and – 1.01 ppm. The peak at – 1.00 ppm is present in both samples and it is probably the same lithium alkoxide aggregate. The other peaks in the mixed samples must relate to some mixed aggregates that are still in this sample, and the other peaks in the lithium alkoxide sample must be other lithium alkoxide aggregates with different aggregation states. These data show that at high O:Li ratios is possible to find both lithium alkoxide aggregates and alkyllithium/lithium alkoxide mixed aggregates.

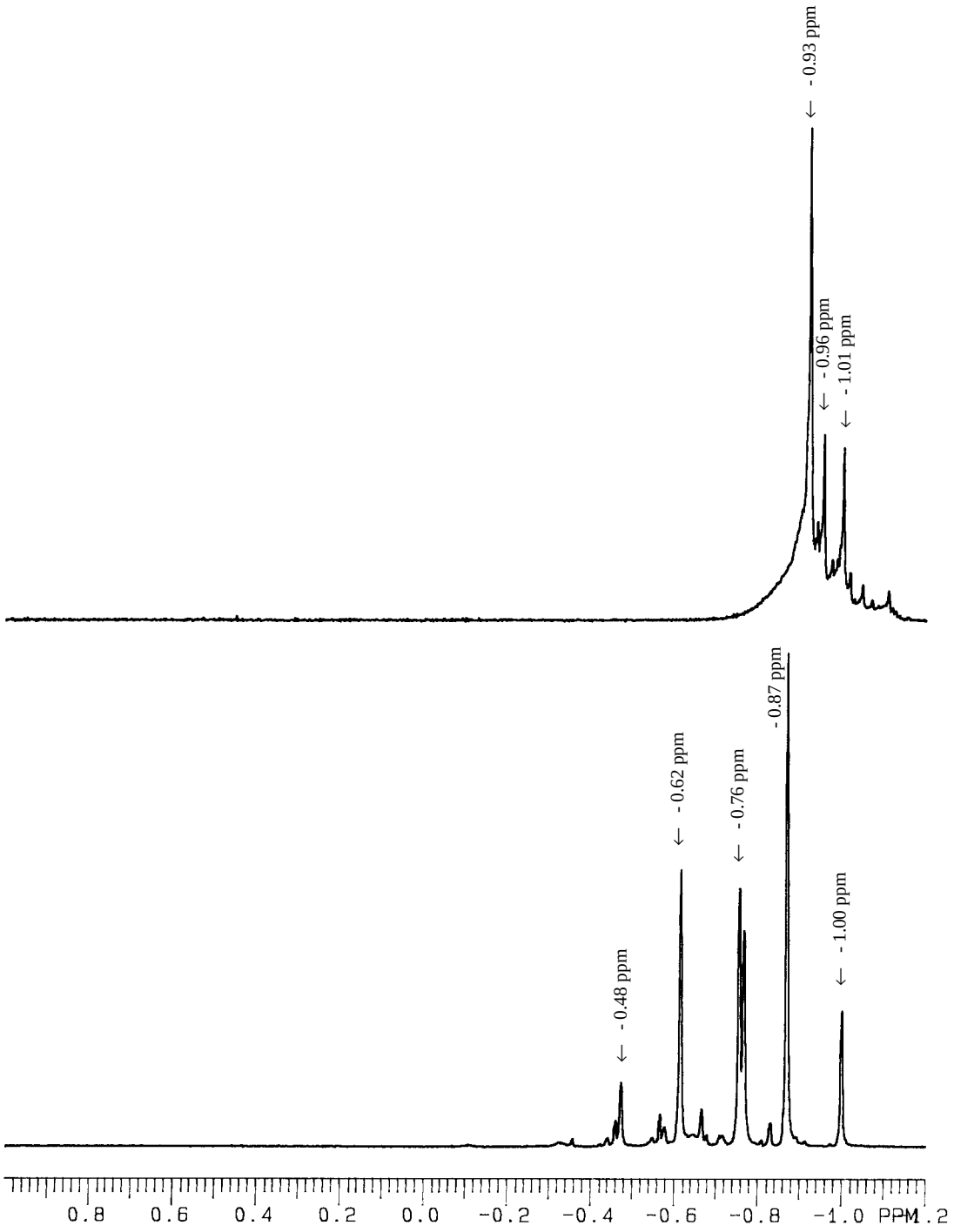


Figure 31 – ^{6}Li NMR spectra of a mixture of 2-ethyl-1-butyllithium and 2-ethyl-1-butanol with O:Li = 1 (bottom) and lithium 2-ethyl-1-butoxide (top) at room temperature.

The ^{1}H NMR spectrum of the lithium 2-ethyl-1-butoxide sample is not shown here because its resolution was very bad due to poor shimming caused by the solid present in the sample. The broad peaks observed were at 3.6, 3.5, 1.3, 1.2 and 0.90 ppm. No peaks were observed between – 0.80 to – 0.90 ppm, which is the alkyl alpha protons region. This was expected because this lithium alkoxide was prepared independently, and, therefore, no alkyl groups should be present. This is the only information that can be obtained from this spectrum.

Figure 32 shows the ^{13}C NMR spectrum of the lithium 2-ethyl-1-butoxide at room temperature. There are more peaks than for just one alkoxide group, which indicates that either more than one aggregate is present or a single aggregate has alkoxide groups in different environments that make these groups magnetically different from one another. The more pronounced peaks in this spectrum are at 67.27, 67.20, 47.90, 47.83, 23.43, 23.17, 10.93 and 10.86 ppm. There also some smaller peaks close to those peaks. All the peaks appear as singlets because of ^{1}H decoupling and also due to the fact that there is no ^{13}C-^{6}Li coupling in the lithium alkoxide. The ^{13}C-^{6}Li coupling is only observed when the carbon nuclei are directly bonded to the lithium nuclei, but in the case of alkoxides, there is an oxygen atom between them.

The presence of multiple peaks was not unexpected for this spectrum because more than one lithium peak was observed for this sample. The data support the presence of multiple lithium alkoxide aggregates in this sample. However, it is difficult to study and determine the aggregation states of these lithium alkoxide aggregates by the same methods used for the alkyllithium aggregates due to the lack of coupling between lithium

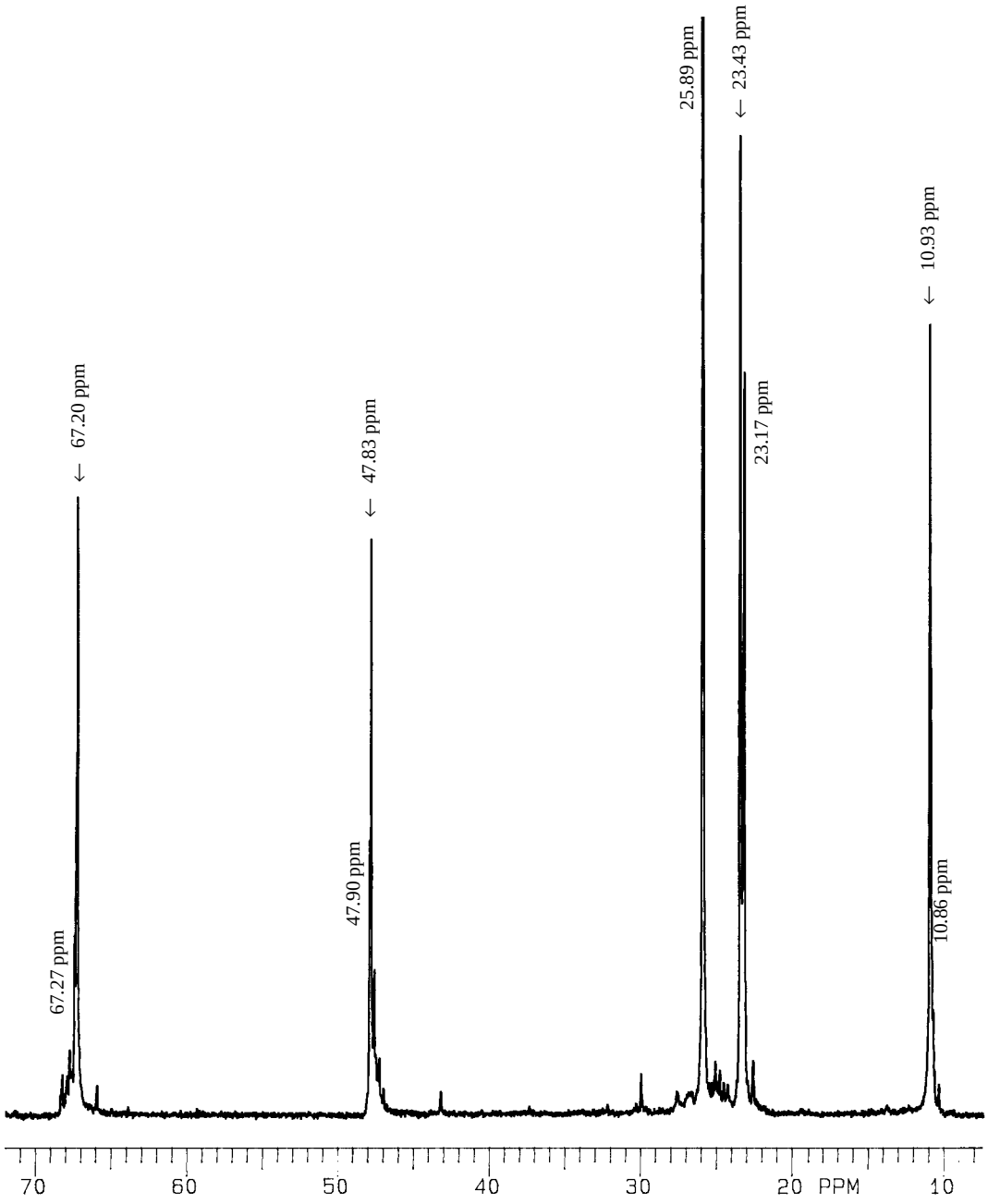


Figure 32 – ^{13}C NMR spectrum of lithium 2-ethyl-1-butoxide at room temperature.

and carbons. The lithium alkoxide aggregates were not studied in much detail in this thesis, but it should be an interesting subject of research looking for new methods of analysis of aggregates in solution.

Summary

This multinuclear NMR study has shown that 2-ethyl-1-butyllithum is a hexameric aggregate in cyclopentane solution at all temperatures from room temperature to – 92.1 °C. Increasing the steric bulk of the straight-chain alkyl group by adding a branch to the beta carbon hindered the formation of larger aggregates at low temperatures, as had been observed for other alkyllithium compounds.[5] In contrast to most straight-chain alkyllithium compounds, for which ^{13}C-^{6}Li coupling could not be observed,[4] the ^{13}C NMR signal for the alpha carbon of 2-ethyl-1-butyllithum resolves into a multiplet at – 10.4 °C with a coupling constant of 3.19 Hz. This is the same coupling constant observed from the ^{13}C satellites in the ^{6}Li NMR spectrum at approximately the same temperature (-16.3 °C). The multiplet observed for the alpha carbon matched the simulation of an alkyl group in a fluxional hexameric aggregate, giving further evidence of the assignment of this aggregate.

The reactions of 2-ethyl-1-butyllithum with 2-ethyl-1-butanol, in which different amounts of alcohol were used as the limiting reagent, produced the formation of lithium alkoxides in a controlled manner. The samples with low O:Li ratio showed, in addition to the original 2-ethyl-1-butyllithum aggregate, the formation of three major alkyllithium/lithium alkoxide mixed aggregates in solution. These were best observed

between the temperatures of 5 °C and – 30 °C. In this temperature range, the interaggregate exchange processes are slowed and better resolution of the peaks is observed in both ^{1}H and ^{6}Li NMR spectra. The ^{13}C NMR spectra showed evidence that at least one of the mixed aggregates formed is possibly an octamer or a nonamer. The other aggregates are ruled out as hexamers and are probably larger aggregates, yet their aggregation states were not determined at this time. The ^{6}Li spectrum at room temperature also showed the presence of small amounts of hydrides that were probably formed due to the heat liberated when the alkyllithium reacts with the alcohol. Proper treatment of the samples, such as controlled heating or exposure to light, could lead to formation of larger amounts of these lithium hydrides.

Mixing the alkyllithium with lithium alkoxide led to the formation of the same type of aggregates in solution as was observed when the alkyllithium was reacted with alcohol. This indicates that the interaggregate exchanges can induce the formation of mixed aggregates, even though the lithium alkoxide compound prepared independently showed very poor solubility in cyclopentane. Due to the low solubility, only small amounts of mixed aggregates were formed in this sample, and a large amount of lithium alkoxide remained as solid floating in the solution.

The sample with higher O:Li ratio (O:Li = 0.6) shows the presence of different aggregates in addition to the ones observed before, for the number of peaks observed increased in all NMR spectra obtained. The original hexameric alkyllithium aggregate is no longer observed. The mixed aggregates that were observed at the low O:Li ratios are present, but in smaller percentages. These new aggregates are very likely to be richer in

alkoxide groups, given that less alkyl groups should be present in solution. This is supported by the upfield shift of the ^{6}Li peaks compared to the alkyllithium peak. However, the aggregation states of the new species in solution were not determined.

The sample with O:Li = 1 showed some remaining alkyl groups present, meaning some mixed aggregates were still found in solution. Some of the peaks observed for this sample are the same ones that had been observed for the sample with O:Li equal to 0.6. The difference is in the intensity of the ^{6}Li peaks, which are greater for the more upfield peaks with the higher O:Li ratio. This is evidence for the argument that the richer the aggregates are in alkoxide groups, the more upfield the ^{6}Li peaks will be shifted. This sample also showed a ^{6}Li peak that can be assigned to an exclusive lithium alkoxide aggregate, because it has the same chemical shift of a peak observed in the independently prepared lithium alkoxide sample. However, this was not the most abundant aggregate in this sample, even though the high O:Li ratio was intended to convert all the alkyl groups in to alkoxides.

Lithium 2-ethyl-1-butoxide showed multiple peaks in the ^{13}C and ^{6}Li spectra, which leads to the conclusion that there is more than just one aggregate in solution at room temperature in spite of the poor solubility of this compound in cyclopentane.

CHAPTER BIBLIOGRAPHY

1. The gNMR 4.0 software was written by Peter H. M. Budzelaar. Published by Cherwell Scientific Publishing Limited, Oxford, 1997.

2. Thomas, R. D.; Clarke, M. T.; Young, T. C., *J. Organometal. Chem.*, **1987**, *328*, 239.

3. Thomas, R. D.; Clarke, M. T.; Jensen, R. M.; Young, T. C., *Organometallics*, **1986**, *5*, 1851.

4. Thomas, R. D.; Jensen, R. M.; Young, T. C., *Organometallics*, **1987**, *6*, 565.

5. Fraenkel, G.; Henrichs, M.; Hewitt, J. M.; Su, B. M.; Geckle, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 3345.

6. Nguyen, H. D. Ph. D. Dissertation, University of North Texas, Denton, TX, 1997.

7. *The Sadtler Guide to Carbon-13 NMR Spectra*; Simons, W. W., Ed.; Sadtler Research Laboratories: Philadelphia, Pennsylvania, 1983.

8. DeLong, G. T.; Hoffmann, D.; Nguyen, H. D.; Thomas, R. D. *J. Am. Chem. Soc.* **1997**, *119*, 11998.

9. Thomas, R. D. In *Isotopes in the Physical and Biomedical Sciences;* Buncel, E.; Jones, J. R., Eds.; Elsevier, Amsterdam, 1991, 2, 367.

10. Thomas, R. D.; Ellington, D. H., *Magnetic Resonance in Chemistry*, **1989**, *27*, 628.

BIBLIOGRAPHY

Bauer, W. In *Lithium Chemistry: A Theoretical and Experimental Overview*; Sapse, A. M.; Schleyer, P. v. R., Eds.; John Wiley & Sons: New York, 1995, 125.

Bauer, W.; Feigel, M.; Muller, G.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1988**, *110*, 6033.

Bauer, W.; Winchester, W.; Schleyer, P. v. R. *Organometallics* **1987**, *6*, 2371.

DeLong, G. T. Ph. D. Dissertation, University of North Texas, Denton, TX, 1992.

DeLong, G. T.; Hoffmann, D.; Nguyen, H. D.; Thomas, R. D. *J. Am. Chem. Soc.* **1997**, *119*, 11998.

DeLong, G. T; Pannell, D. K.; Clarke, M. T.; Thomas, R. D. *J. Am. Chem. Soc.* **1993**, *115*, 7013.

Ellington, D. H. Ph. D. Dissertation, University of North Texas, Denton, TX, 1990.

Fraenkel, G.; Henrichs, M.; Hewitt, J. M.; Su, B. M.; Geckle, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 3345.

Fraenkel, G.; Henrichs, M.; Hewitt, J. M.; Su, B. M.; *J. Am. Chem. Soc.* **1984**, *106*, 255.

Fraenkel, G.; Hsu, H.; Su, B. M. In *Lithium: Current Applications in Science, Medicine and Technology*; Bach, R. O., Ed.; John Wiley & Sons: New York, 1985, 273.

Gorrell, I. B. *Annu. Rep. Prog. Chem., Sect. A: Inorg. Chem.* **1994**, *90*, 3.

Kottke, T.; Stalke, D. *Agnew. Chem. Int. Ed. Engl.*, **1993**, *32*, 580.

Nguyen, H. D. Ph. D. Dissertation, University of North Texas, Denton, TX, 1997.

Olsher, U.; Izatt, R. M.; Bradshaw, J. S.; Dalley, N. K. *Chem. Rev.* **1991**, *91*, 137.

Schiemenz, B.; Power, P. P. *Agnew. Chem. Int. Ed. Engl.*, **1996**, *35*, 2150.

Schleyer, P. v. R.; Gregory, K.;Snaith, R. *Adv. Inorg. Chem.* **1991**, *37*, 47.

Seebach, D. *Angew. Chem, Int. Ed. Engl.* **1988**, *27*, 1624.

The Sadtler Guide to Carbon-13 NMR Spectra; Simons, W. W., Ed.; Sadtler Research Laboratories: Philadelphia, Pennsylvania, 1983.

Thomas, R. D. In *Isotopes in the Physical and Biomedical Sciences;* Buncel, E.; Jones, J. R., Eds.; Elsevier, Amsterdam, 1991, 2, 367.

Thomas, R. D.; Clarke, M. T.; Jensen, R. M.; Young, T. C. *Organometallics* **1986**, *5*, 1851.

Thomas, R. D.; Clarke, M. T.; Young, T. C., *J. Organometal. Chem.*, **1987**, *328*, 239.

Thomas, R. D.; Ellington, D. H., *Magnetic Resonance in Chemistry*, **1989**, *27*, 628.

Thomas, R. D.; Huang, H. *J. Am. Chem. Soc.* **1999**, *121*, 11239.

Thomas, R. D.; Jensen, R. M.; Young, T. C., *Organometallics* **1987**, *6*, 565.

Thornton, T. L. Master Thesis, University of North Texas, Denton, TX, 1997.

Van Geet, A. L. *Anal. Chem.* **1968**, *40*, 2227.

Wakefield, B. J., *The Chemistry of Organolithium Compounds*, Pergamon Press, Oxford, 1974.

Wakefield, B. J., *Organolithium Methods*, Academic, Oxford, 1988.

Wardell, J. L., *Comprehensive Organometallic Chemistry*, Wilkinson, G. Ed.; Pergamon Press: New York, 1982, Vol 1, 43.

Weiss, E. *Angew Chem., Int. Ed. Engl.* **1993**, *32*, 1501.